November 18, 2005

Mr. Michael Gallagher
PBT Coordinator
State of Washington Department of Ecology
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RE: Inclusion of Tetrabromobisphenol A in the Department of Ecology's Proposed Rule regarding Persistent Bioaccumulative Toxins (PBTs) (Chapter 173-333 WAC).

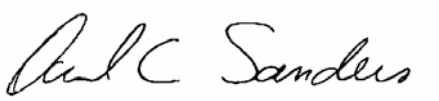
Dear Mr. Gallagher:

The Bromine Science and Environmental Forum (BSEF) is a global industry association composed of the major manufacturers of brominated flame retardants and our mission is to further the scientific understanding of our products. As such, BSEF and its member companies have sponsored numerous studies on the potential health and environmental effects of our products, and we have engaged the services of individuals with in-depth knowledge of the toxicology of our products. Additional studies of TBBPA's potential for environmental persistence are on-going.

BSEF submits the attached comments on the inclusion of tetrabromobisphenol A (TBBPA) in the Department of Ecology's proposed rule regarding Persistent Bioaccumulative Toxins (PBTs) (Chapter 173-333 WAC).

TBBPA does not meet the criteria set out for PBT substances in the Department's proposed rule, and should be deleted from the list of substances proposed for inclusion.

Sincerely,



Raymond B. Dawson, PhD.
Chairman
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Director, North America
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Enclosure: Comments
TBBPA IUCLID file

TETRABROMOBISPHENOL A (TBBPA)

The Department of Ecology proposes that a substance would be considered persistent, bioaccumulative and toxic if:

- Its half-life in water, soil or sediment is > 60 days;
- Its bioconcentration/bioaccumulation factor is > 1000; and
- It is a known carcinogen, reproductive or neurologic toxicant, has a reference dose (RfD) of < 0.003 mg/kg/d, or is toxic to fish on chronic exposure.

Our comments on the above proposed criteria are submitted under a separate cover.

TBBPA does not meet the Department's proposed criteria for a persistent, bioaccumulative and toxic substance, and should be removed from the proposed rule. The data supporting its removal is presented below and in the attached IUCLID file.

Persistence

TBBPA was determined not to be 'readily biodegradable' in the MITI test; e.g. it was not degradable by sewage microbes within a 28 day period when tested under stringent conditions. However, TBBPA was degradable under more environmentally realistic conditions, and therefore should not be considered persistent. Aerobic and anaerobic studies indicate a soil half-life of approximately 50 days. An aerobic sediment/water degradation study produced a half-life of approximately 67 days, and half-lives of 28 and 40 days were estimated from an anaerobic sediment study. TBBPA also appears rapidly photodegradable in water, with half-lives ranging from 16-360 minutes depending on pH.

These studies are summarized as follows and in the attached IUCLID file.

<u>Anaerobic Biotransformation in Estuarine Sediments</u>

Degradation of TBBPA was studied in anoxic estuarine sediments under methanogenic or sufate-reducing conditions. Sediment grab samples were collected from the Arthur KIll tidal strait located between Staten Island and New Jersey, U.S. Anaerobic enrichments used in the test contained 25% v/v live Arthur Kill sediment. The nominal concentration of TBBPA tested in the enrichments was 225-275 uM. Greater than 95% of the TBBPA partitioned to the sediment.

Under methanogenic conditions, initial TBBPA loss was observed within 14 days with a nearly concomitant stoichiometrically equivalent amount of bisphenol A (BPA) produced. Near complete loss of TBBPA was seen within 55 days. Based on Fig 1 of the publication, TBBPA's half-life is estimated to be approximately 28 days.

Under sulfate-reducing conditions, degradation of TBBPA commenced after a lag period of 28 days and was virtually complete within 112 days. BPA was not detected until after there had been substantial loss of TBBPA (after 70 days). Based on Fig 1, TBBPA's half-life is estimated to be approximately 40 days.

No loss of TBBPA was observed in the autoclaved controls.

Under methanogenic and sulfidogenic conditions, complete dehalogenation of TBBPA to BPA, with no further degradation of BPA, was observed. Dehalogenation of TBBPA to BPA was much slower in the sulfate-reducing enrichments than in the methanogenic enrichments. TBBPA's half-life is estimated to be 28 (methanogenic) and 40 (sufidogenic) days (Voordeckers J, Fennell D, Jones K, Haggblom M. 2002. Anaerobic biotransformation of tetrabromobisphenol A, tetrachlorobisphenol A, and bisphenol A in estuarine sediments. Environ. Sci. Technol. 36:696-701).

56-Day Sediment/Water Microbial Degradation

This study was sponsored by the Brominated Flame Retardant Industry Panel (BFRIP).

The biodegradability of 14C-TBBPA was tested under aerobic conditions in a sediment/water microbial test system using natural river sediment and water. The test conditions were pH 5.5, field moisture capacity 15.9%, temperature 24-26 degrees C, and the composition of the soil (6.8% carbon) was 92% sand, 6% silt, and 2% clay.

TBBPA biodegraded at all tested concentrations (0.01, 0.1 and 1 mg/L). Half-lives calculated for TBBPA in the sediment/water microbial test systems ranged between 48 days at 0.01 ug/L concentration and 84 days at the 1 mg/L concentration with apparent correlations between half-life and TBBPA concentration and half-life and microbial population. The half-life in sterile sediment was extrapolated to be 1300 days, indicating that the degradation observed in the active test systems was due to microbial degradation rather than physical processes.

Less than 8% of the applied radioactive carbon from TBBPA was recovered in the volatile traps indicating partial degradation to C02.

Filtered water contained less than 5% of the applied radioactivity.

The amount of radioactivity observed to be remaining in the sediment at test termination, 44.7, 64.2, and 60.8% in the 0.01, 0.1 and 1 mg radioactive TBBPA/L treatments, respectively, was comparable to the amounts reported in the aerobic degradation study in soil.

Half-lives calculated for TBBPA in the sediment/water microbial test systems ranged between 48 and 84 days, with an apparent correlation between half-life and concentration of TBBPA and half-life and microbial population.

Fackler P. 1989. Tetrabromobisphenol A. Determination of biodegradability in a sediment/water microbial system. SLS Report 89-8-3070. Springborn Life Sciences, Inc. Wareham, Massachusetts.

WHO 1995. Tetrabromobisphenol A and Derivative. World Health Organization International Programme on Chemical Safety Environmental Health Criteria Document Number 172. Geneva.)

64-Day Aerobic Soil Degradation

This study was performed according to Good Laboratory Practices and according to US EPA OPPTS guidelines. Sponsor: Brominated Flame Retardant Industry Panel (BFRIP).

The biodegradability of 14C-TBBPA was tested under aerobic conditions in three soil types, i.e., Massachusetts sandy loam, a California clay loam, and Arkansas silty loam. The three soil types contained: sand (83%)-silt (13%)-clay (4%), sand (16%)-silt (58%)-clay (26%), and sand (43%)-silt (24%)-clay (33%), respectively. Thin layer chromatography (TLC) showed biodegradation of TBBPA in all soil types. Less than or equal to 6% of the applied radioactive TBBPA was recovered in the volatile traps, indicating partial degradation to C02. Results of the TLC analysis indicated variable degradation rates of TBBPA, which were dependent on soil type. After 64 days, the amount of TBBPA remaining in the soils ranged from 36 to 82%, with the highest level in sandy loam soil and the lowest in the silty loam soil. Degradation products (2 or 3 depending on soil type) were not specifically identified, but the dimethyl and diethyl derivatives of TBBPA were ruled out based on TLC characteristics of authentic standards.

Fackler P. 1989. Determination of the biodegradability of tetrabromobisphenol A in soil under aerobic conditions. SLS Report 88-11-2848. Springborn Life Science, Inc. Wareham, Massachusetts.

Photolysis in Water

Eriksson et al. (2004) reported the photodegradation of TBBPA in water at various pHs (5.5-10) after UV irradiation.

The rates of decomposition were determined at a concentration of 77 uM in water. The illumination time was 50 minutes. Fluorescent tubes (Philips TL 20W/09N) provided the irradiation, and were intended to represent the range of solar UV wavelengths, which penetrate the full atmosphere.

TBBPA's rate of decomposition ranged from 0.7 (pH=10) to 0.033 (pH=5.5) kx103/s. Its half-life ranged from 16 (pH=10) to 350 (pH=5.5) minutes; TBBPA's half-life at pH 7.4 = 24 minutes. The disappearance quantum yield ranged from 0.045 (pH=10) to 0.018

(pH=5.5). The quantum yield was defined as the ratio between the number of reacted molecules per unit time and unit volume and the total number of photons absorbed per unit time and unit volume.

The maximum absorption was found at 310 nm at all pHs except for pH 6.1 and 5.5 where the maximum absorbance was at 290 nm.

TBBPA decomposed via cleavage between the isopropyl group and one of the benzene rings. The main decomposition products were 4-(2-hydroxyisopropyl)-2,6-dibromophenol; 4-isopropylene-2,6-dibromophenol; and 2,6-dibromo-4-isopropylene.

The data indicated that TBBPA was readily photodegraded in aqueous solution. Degradation rates were sensitive to pH.) Laboratory studies indicate TBBPA has the potential for degradation in the environment, and therefore is not persistent. Aerobic and anaerobic studies indicate a soil half-life of approximately 50 days. An aerobic sediment/water degradation study produced a half-life of approximately 67 days, and half-lives of 28 and 40 days were estimated from an anaerobic sediment study. TBBPA also appears rapidly photodegradable in water, with half-lives ranging from 16-360 minutes depending on pH.

Eriksson J, Rahm S, Green N, Bergman A, Jakobsson E. 2004. Photochemical transformations of tetrabromobisphenol A and related phenols in water. Chemosphere 54: 117-126.

Photolysis in Water or Silica Gel

TBBPA's calculated half-life in water by UV radiation was 10.2 days in spring, 6.6 days in summer, 25.9 days in autumn, and 80.7 days in winter. The half-life of TBBPA adsorbed onto silica gel and exposed to UV radiation was 0.12 days (reported in WHO 1995).

Bioconcentration

TBBPA’s measured BCF in fish is < 500. With two hydroxyl groups, TBBPA is readily metabolized to more water soluble conjugates and rapidly eliminated. Studies confirm that TBBPA is not bioaccumulative and is rapidly eliminated.

Several studies have investigated TBBPA's potential for absorption and elimination in environmentally relevant species.

After exposure to TBBPA in water, fish rapidly reached steady-state tissue concentrations with measured BCFs of < 500. Fish also rapidly eliminated TBBPA once removed to fresh water.

After oral exposure of quail, TBBPA was rapidly eliminated via bile and excreted in feces, and transfer to egg yolks was low. After egg yolk injection, TBBPA's transfer to the growing embryo was low, and that amount transferred was readily excreted by the embryo. Thus, the risk for bioaccumulation or embryonic exposure following dietary intake in laying birds is expected to be low.

After intention ingestion, TBBPA was not detected in human sera at any time point. Only glucuronide or sulfate conjugates were detected, and were rapidly eliminated.

Based on these studies, TBBPA has little potential to bioconcentrate or bioaccumulate in humans, fish, or birds. This is likely related to the organisms' ability to metabolize TBBPA to readily eliminated forms.

Rat Absorption, Metabolism, Elimination Study (^{14}C-TBBPA)

In the rat, TBBPA was readily absorbed, metabolized and eliminated within 72 hours after oral dosing. Recovery of ^{14}C-activity in the conventional (n=10) and bile-cannulated (n=8) rat administered a single oral dose of ^{14}C-TBBPA was 92 and 98.5% of the dose, respectively, by 72 hours post-dosing. Owing to the extensive elimination, total tissue retention at 72 hours was limited. In the conventional rat, 2% of the dose was retained in the tissues, but <1% in the cannulated rat at 72 hours. Essentially no deposition of TBBPA was detected in adipose tissue, heart, spleen, testis or thymus (<0.0005% of dose).

The primary route of elimination was the feces; only negligible amounts were detected in urine. Glucuronic acid and sulphate ester conjugates were detected in bile; however, the parent molecule was the predominant form found in feces due to deconjugation by intestinal bacteria (Haak et al. 2000; Larsen et al 1990).

Earlier work concluded that in rats, after oral dosing, approximately 95 percent of the administered material was found in the feces and less than 1.1 percent in the urine within 72 hours. Blood and tissue levels were extremely low at all time points measured. The half-life in the blood was about 20 hours; the maximum half life in any tissue was less than 3 days. Because of the short half-life, the small amounts of TBBPA absorbed would have relatively little persistence or accumulation in mammalian systems (WHO 1995).

Larsen, G. et al, Organohalogen Compounds, 31, 413-416, 1999

Haak H, Larsen G, Bergman A and Orn U. 2000. Metabolism, excretion and distribution of the flame retardant tetrabromobisphenol A in conventional and bile-duct cannulated rats. Xenobiotica, 2000, 30,9,881-890.

WHO 1995. Tetrabromobisphenol A and Derivative. World Health Organization International Programme on Chemical Safety Environmental Health Criteria Document Number 172. Geneva.

Human Metabolism and Clearance

In humans, TBBPA is rapidly metabolized. A single oral dose of 0.1 mg/kg was administered in a gel capsule to 3 male and 2 female volunteers. Urine and blood concentrations of TBBPA and its metabolites were determined by LC/MS-MS.

The parent TBBPA molecule was not detected in plasma at any time point. The glucuronide and sulfate conjugates of TBBPA were detected in blood and urine. TBBPA-glucuronide was detected in all volunteers, whereas TBBPA-sulfate was detected in only 2 of the 5. Maximum plasma concentrations of the TBBPA-glucuronide (10-15 pmol/ml) were found 2 hrs post-dosing. The glucuronide conjugate was cleared from the blood with an apparent half-life of 26 hrs. In the 2 individuals where the sulfate conjugate was detected, maximum concentration of the sulfate conjugate in the 2 individuals were detected 4 hr post dosing and declined to the limit of detection after 8 hrs. Only TBBPA-glucuronide was detected in the urine. Approx. 25% of the administered dose was eliminated in the urine. Most of the TBBPA-glucuronide was thought to be eliminated in the feces (Dekant et al. 2005)

Dekant W, Voelkel W, Schauer U. Toxicokinetics of tetrabromobisphenol A in human subjects. Abstract No. 1239. 2005 Itinerary Planner. New Orleans, LA: Society of Toxicology.

BCF in Japanese Carp

The bioconcentration of TBBPA was evaluated in Japanese carp following an 8 week exposure period at concentrations of 8 or 80 ug/L. The BCF was 30-341 at 80 ug/L and 52-485 at 8 ug/L. The LC50 in killifish was determined to be 8.2 mg/L at 48 hours (reported in WHO 1995).

CITI 1992. Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan. Compiled under the supervision of Chemical Products Safety Division, Basic Industries Bureau, Ministry of International Trade & Industry, Japan. Edited by Chemicals Inspection & Testing Institute, Japan. Published by Japan Chemical Industry Ecology-Toxicology & Information Center.

Reproduction and Distribution in Japanese Quail

The potential for TBBPA to affect reproduction variables in adult Japanese quails following *in* ovo exposure as well as TBBPA's distribution in eggs, embryos and laying birds was investigated using 14C-labelled material. Uptake of 14C-TBBPA was studied in 6- and 9-day-old quail embryos, by beta-spectrometry, following egg-injection (1.9 ug/g egg) on day 3. TBBPA's distribution in quail embryos (1.9 ug/g egg) and adult females (oral and intravenous, 250 ug/bird) was studied using tape-section autoradiography following a single dose. The potential for effects on male sexual

behavior, testis weight, plasma testosterone concentration, egg-laying, and gross morphology of the oviducts was evaluated in adult birds following embryonic exposure (15 ug/g egg).

The embryonic uptake of TBBPA was low (< 1% of the radiolabel) after yolk injection on day 3 of incubation. Its distribution pattern was characterized by a strong retention in the yolk at all time points, although evidence for metabolism was detected (labeling in the liver, bile and allantoic fluid). Thus, TBBPA's transfer to the embryo from the yolk was low, and any transferred TBBPA was rapidly metabolized and readily excreted.

In laying quail, orally or intravenously administered TBBPA was rapidly eliminated via bile and excreted in feces, and transfer to egg yolks was low. Thus, TBBPA was readily excreted by the laying female as well as by the growing embryo, and consequently, the risk for embryonic exposure following dietary intake in laying birds is expected to be low.

In ovo exposure to TBBPA (15 ug/g egg) did not cause estrogen-like effects in the adult quail. Egg-laying was not affected in female birds, and no effect in male quail on sexual behavior, testis weight or plasma testosterone was detected. (Halldin K et al. 2001.)

Another study by the same group also reported that TBBPA (45 ug/g quail egg) did not induce estrogenic-like effects (Berg et al. 2001)

Halldin K, Berg C, Bergman A, Brandt I and Brunstrom B. 2001. Distribution of bisphenol A and tetrabromobisphenol A in quail eggs, embryos and laying birds and studies on reproduction variables in adults following in ovo exposure. Arch Toxicol 75:597-603.

Berg C, Halldin K, and Brunstrom B. 2001. Effects of bisphenol A and tetrabromobisphenol A on sex organ development in quail and chicken embryos. Environ Toxicol Chem. 2001 Dec;20(12):2836-40.

Toxicity, Mammalian

TBBPA is not acutely toxic or irritating to the skin and eye. It does not elicit delayed skin hypersensitivity. It is not mutagenic. It is not a developmental toxicant and does not affect reproduction at doses up to 1000 mg/kg bw. It produces essentially no effects when administered repeatedly at doses up to 1000 mg/kg/d, and has been tested in several different species. It is rapidly metabolized and eliminated as glucuronide and sulfate conjugates, and is not expected to bioaccumulate.

The most relevant repeated dose studies are summarized below. Additional studies can be found in TBBPA's IUCLID file.

Rat 90-Day Subchronic Oral (Gavage)

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and OECD guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel.

This study was conducted to evaluate the subchronic toxicity of TBBPA in CD® [Crl: CD® (SD) IGS BR] rats. The study consisted of three treatment groups and one vehicle (corn oil) control group (ten rats/sex/group). Recovery animals (five rats/sex) were included in the control and high-dose group and evaluated over a 6-week post-treatment period. TBBPA was administered orally by gavage daily for 13 weeks at dose levels of 0, 100,300, and 1000 mg/kg/day at a constant volume of 5 mL/kg/day. The control animals received the vehicle at the same volume and dosing regimen as the treated groups. Animals were observed daily cage side for survivability, injury, and availability of feed and water. Other observations conducted weekly during the study included detailed physical and neurobehavioral evaluations, and measurements of body weights and food consumption. A Functional Observational Battery (FOB) was conducted pretest and at Week 12. Motor activity (MA) was also evaluated during Week 12. Ophthalmoscopic examinations were conducted pretest, study termination, and following recovery .Other evaluations conducted at termination and following recovery included: hematology, clinical chemistry , urinalysis, organ weights, and pathological examinations (macroscopic and microscopic). Thyroid hormone levels [Thyroid Stimulating Hormone (TSH), T3 (3,5,3' -triiodothyronine), and T4 (thyroxine or 3,5,3'5'-tetraiodothyronine)] were evaluated of animals at 33 days and at termination. These same hormone levels were evaluated following recovery.

Homogeneity of the dosing suspensions at the low and high concentration levels was determined on mixes used the first week of study. Mean concentration recoveries from the periodic analyses of dosing suspensions used on study were 102.5%, 110.2%, and 106.8% of nominal for the l00, 300, and 1000 mg/kg/day groups, respectively.

A total of six females (two control and four in the 1000 mg/kg/day group) died or were euthanized in extremis. The mortality/morbidity seen in these groups was considered related to dosing injury and not treatment related.

No effect of treatment was seen in clinical or neurobehavioral evaluations, body weights, food consumption, ophthalmological examinations, MA, FOB evaluations, hematology or urinalysis evaluations. Likewise, no effect of treatment was evident from organ weights, or from the macroscopic or microscopic examinations.

After 90 days of dosing, total bilirubin values were statistically higher than the control means (males: 0.14 ± 0.05; females: 0.13 ± 0.05) in males in the 1000 mg/kg/day dose (0.34 ± 0.024) ($p<0.01$) group and in females in the 300 (0.19 ± 0.03) ($p<0.05$) and 1000 mg/kg/day (0.2 ± 0.06) groups ($p<0.01$). Mean serum alkaline phosphatase (ALP) levels

after 90 days of dosing in the female 1000 mg/kg/day (98.9 ± 49.47) group was statistically higher than that of the control mean (58.4 ± 28.46) ($p<0.05$). A slight increase, but non-statistically different, was also observed in males. Although these differences were considered possibly due to test article administration, neither of these changes was of sufficient magnitude as to be biologically or toxicologically meaningful or adverse. Serum bilirubin and ALP levels in control and treated groups of both sexes were comparable after the end of the recovery period.

With respect to serum hormone levels, mean TSH and T3 levels were statistically comparable between control and treated animals at all time points (Day 33, terminal and recovery euthanasia). Mean T4 levels were statistically lower than the control mean (Day 33: 4.96 ± 0.84; terminal: 5.09 ± 0.80) in the 100 (Day 33: 3.66 ± 0.88; terminal: 3.27 ± 0.67), 300 (Day 33: 3.42 ± 0.71; terminal: 2.61 ± 0.87) and 1000 (Day 33: 3.39 ± 0.55; terminal: 3.09 ± 0.91) mg/kg/day male dose groups at days 33 and 90 ($p<0.01$). Mean T4 1evels were also statistically lower than the control mean (4.27 ± 0.96) in females in the l00 (3.31 ± 1.08), 300 (3.24 ± 0.85) and 1000 (3.33 ± 0.84) mg/kg/day dose groups at Day 33 ($p<0.05$). Mean T4 1evels in all female dose groups were statistically comparable to the control mean at Day 90. At the recovery euthanasia, mean T4 1evels were comparable in the control and 1000 mg/kg/day male and female groups. The change in T41evels seen in the 1000 mg/kg/day group was reversible and levels comparable to control were seen following recovery.

The decrease in serum T 4 levels was considered a possible effect of test article administration. TBBPA has been shown to competitively displace T4 from transthyretin (TTR), a major serum T4-binding protein in the rat, in vitro (Meerts et al. 2000. Toxicological Sciences, 56,95-104). That portion of serum T4 displaced from its binding site would be available for metabolism and elimination, thereby leading to a decrease in serum levels. The half-life of T4 in the rat is short due to its transport by TTR, and thus this species is sensitive to perturbations in T4 levels. For example, the plasma T4 half-life in rats is 12-24 hours while T4's half-life in humans is 5-9 days (Capen, C. 1996. Chapter 21. Toxic Responses of the Endocrine System. In: Casarett & Doull's Toxicology, The Basic Science of Poisons. Fifth Edition. Ed. Curtis Klaassen. McGraw-Hill, New York. 474-006). In humans circulating T4 is bound primarily to thyroxin binding globulin, but this high affinity binding protein is not present in rodents. This mechanism, displacement of T4 from TTR-binding by TBBPA with subsequent metabolism and elimination in the liver, may account for the decreased mean serum T4 levels in treated animals. Because the decrease in T4 1evels was not of sufficient magnitude to alter mean serum TSH or T3 levels, thyroid histopathology, thyroid weight, or other parameters indicative of thyroid pathology (e.g. body weight, etc.), the decrease in serum T4 1evels was not considered adverse. The reduction in serum T4 1evels was not accompanied by evidence of toxicity or adverse effects, and the animals were clinically normal.

Thus, in this rat 90-day oral toxicity study with TBBP A, the No Observed Adverse Effect Level (NOAEL) was 1000 mg/kg/day, the highest dose tested. No effect on mortality, clinical signs, body or organ weights, histopathology, urinalysis,

ophthalmology, FOB, MA, serum TSH, serum T3 or serum chemistries was observed. Differences were observed for bilirubin and ALP, but neither of these changes was found to be biologically or toxicologically meaningful or adverse. Serum T4 levels were decreased in treated animals, but the decrease was not of sufficient magnitude to induce adverse effects.

Schroeder R. 2002. A 90-day oral toxicity study of tetrabromobisphenol A in rats with a recovery group. Study Number: 474-006. MPI Research, Inc. Mattawan, MI.

Rat Prenatal Developmental

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and OECD guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel (BFRIP)

The objective of this study was to provide information concerning the effects of oral treatment of the pregnant rat with TBBPA on the developing organism. This included death, structural abnormalities or altered growth, and assessment of maternal effects. This study consisted of 3 treatment groups and 1 vehicle (corn oil) control group (25 mated female rats/group). Female CD® rats [Crl: CD® (SD) IGS BR] were mated in-house and received TBBPA at dose levels of 0, 100, 300 and 1000 mg/kg/d at a constant volume of 5ml/kg. The control animals received the vehicle at the same volume and dosing regimen as the treated groups. The test article was administered orally by gavage as a single daily dose. Dosing initiated on Day 0 of gestation and continued through to include Day 19 of gestation. The day on which evidence of mating was observed was considered Day 0 of gestation. Observations of the dams included clinical signs, gestational body weights, and food consumption. Females were euthanized on Day 20 of gestation and given a postmortem macroscopic examination. Gross lesions were saved in 10% neutral buffered formalin for possible future examination. Gravid uterine weights and liver weights were recorded. Litters were delivered by cesarean section. The total number of corpora lutea, uterine implantations, early and late resorption, viable and nonviable fetuses, and the sex and individual weights of fetuses were recorded. Al fetuses were given a gross external examination for malformations and variations. Approximately one-half of the fetuses in each litter were fixed in Bouin's solution, and the remaining fetuses were skinned and preserved in alcohol. Bouin's-fixed fetuses from the control and all treated groups were examined for visceral abnormalities (freehand razor blade sectioning procedure), and the remaining fetuses from all groups were stained with Alizarin Red S and Alcian Blue and evaluated for skeletal/cartilaginous malformations and ossification variations. The maternal Day 20 gestation examinations and cesarean sections and subsequent fetal evaluations were performed blind to treatment.

Pretest analyses confirmed that the suspensions as prepared were homogeneous and stable for a t least 14 days when stored refrigerated. Periodic analysis of the dosing suspensions showed levels ranged from 88 - 113% of nominal and confirmed that animals were receiving the appropriated dose levels.

No test article-related mortality occurred. The death of 1 animal in the 300 mg/kg/day group on Gestation Day 5 was due to an intubation injury. All other animals survived to scheduled euthanasia.

Salivation was seen among the TBPPA-treated animals, occurring most frequently at the 300 an 1000 mg/kg/day dose levels. Because of its sporadic occurrence, this was not considered to represent a direct effect of TBBPA, but more likely was in response to the taste of the residual amounts of the test article on the dosing catheter. No other effects of treatment were seen on clinical examination. No effect of treatment was evident from gestational parameters (body weight, body weight gain, or food consumption), uterine implantation data, liver weights, or necropsy findings. No effect of treatment was evident on fetal body weights, fetal sex distribution, or on fetal external, visceral or skeletal examinations. The NOAEL in this oral developmental toxicity study in rats with TBBPA for maternal and developmental toxicity was 1000 mg/kg/d, the highest dose level tested.

Schroeder, R. 2001. An oral prenatal developmental toxicity study with tetrabromobisphenol A in rats. Study No. 474-005. MPI Research, Mattawan, MI.

Rat 2-Generation Reproduction Study (BFRIP)

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel (BFRIP)

The objective of this reproduction study was to provide information concerning the effects of TBBPA over the course of two generations (P and F1) and the growth and development of the offspring (F1 and F2. A developmental neurotoxicity/neuropathology assessment was also conducted on the F2 offspring. The study consisted of three treatment groups (10, l00 and 1000 mg/kg/day) and a vehicle (corn oil)-treated control group (30 CD® [Crl: CD® (SD) IGS BR] Sprague-Dawley rats/sex/group/generation). TBBPA was administered orally via gastric intubation. Animals were treated seven days a week throughout the study. Dosing suspensions were prepared fresh weekly. Parental animals were treated for at least 10 weeks prior to mating (premating treatment period) to produce the F1 and F2 litters. In the developmental neurotoxicity/neuropathology (DNT/NP) component, F2 pups were randomly selected to continue on study for the following evaluations (unique sets of animals [10 pups/sex/group] were randomly selected for each assessment): PND 60 brain weights, PND 60 perfusion and neuropathology, special detailed clinical examinations (PND 4, 11, 21, 35, 45, and 60),

motor activity [MA] (PND 13, 17, 21, and 60), auditory startle habituation [ASH] (PND 22 and 60), and learning and memory [L&M] (PND 22, 60 and 110). Additionally, 10 F2 pups/sex/group were selected randomly on PND 11 for collecting, weighing, and preserving of the brains.

For breeding of the P and F1 generations, one male was paired with one female from the same treatment group continuously until mating occurred or for 14 consecutive days. The day of mating evidence was considered Day 0 of gestation. During mating of the F1 generation, cohabitation of littermates was avoided. Females delivered and nursed litters over a 21-day lactation period. On Day 4 of lactation all litters were culled if necessary to 8 pups (F1) or 10 pups (F2) with sex distribution equalized, when possible. Litters with fewer pups than required at culling were not adjusted.

At weaning of each F1 litter, at least one pup/sex/litter was selected to continue on study as the F1 parental generation (30 pups/sex/group). These pups started treatment on PND 22. The premating period formally initiated after the last litter weaned. Thus, there was a maximum of two weeks difference in age for the F1 animals within each treatment group at initiation of the premating growth period.

Detailed clinical examinations, body weights, and food consumption were recorded periodically throughout the study for the P and F1 parental animals. Estrous cyclicity was evaluated in the P and F1 females the last three weeks of the premating period, and these evaluations continued until the female was confirmed mated or to the end of the mating period. Females were allowed to deliver and nurse the litter to weaning. Litters were evaluated at birth and throughout the lactation period. Each pup was individually identified at birth (paw tattoo), sexed, examined externally for defects, and weighed. All pups were monitored for appearance, growth, and survival throughout the lactation period. Clinical examinations, body weights, food consumption, and occurrence of maturation landmarks (vaginal opening [VO] and preputial separation [PS]) were recorded for F) parental animals.

Several days before terminal euthanasia of the P and F1 animals, blood was collected from 10 randomly selected animals/sex/group and analyzed for thyroid hormone levels (TSH, T 3 and T 4). At necropsy, P and F1 animals received a macroscopic examination and reproductive tissues and other designated tissues were taken, weighed, and preserved. Reproductive tissues were evaluated microscopically for all P and F1 animals in the control and 1000 mg/kg/day groups. Microscopic examinations were also performed for reproductive tissues of the few low- and mid-dose P and F1 animals that failed to mate, conceive or sire. Gross lesions were also examined microscopically for all parental animals. Sperm evaluations (motility, caudal epididymal sperm counts, homogenization-resistant testicular sperm head counts, and morphology) for P and F, males and a count of primordial follicles were conducted for P and F1 females. The latter evaluations were conducted only in the control and 1000 mg/kg/day groups. At weaning, the unselected F1 pups and one F2 pup/sex/litter were euthanized, necropsied, specific organs weighed (brain, spleen, and thymus), and gross lesions preserved.

In the DNT/NP component, brains from F2 pups euthanized on PND 11 (l0/sex/group) were weighed, and preserved in fixative for neuropathological evaluation and morphometric measurements. These examinations were initially conducted in the control and high-dose animals and were expanded to include the lower dose groups. F 2 pups retained post-weaning were observed twice daily cage side for mortality and were weighed and given detailed clinical examinations periodically during the study. Sexual maturation (VO and PS) was evaluated for the 40 animals/sex/group retained for the neurobehavioral assessments (i.e., special clinical examinations, MA, L&M, and ASH). These animals were euthanized after all the behavioral tests had been completed. At termination, all F2 animals were weighed, given a detailed clinical examination and necropsied. The F2 animals euthanized on PND 60 for neuropathological evaluation were anesthetized with sodium pentobarbital and perfused with 3% paraformaldehyde and 3% glutaraldehyde. The whole brain, sections of the spinal cord, and selected peripheral nerves were collected and processed for neuropathological examination in the control and 1000 mg/kg/day groups.

Dosing formulations were homogeneous at the batch size prepared and stable when refrigerated to 14 days. Mean recoveries from the periodic analyses of dosing suspensions used on study were 101 %, 99%, and 105% of nominal for the 10, l00, and 1000 mg/kg/day groups, respectively.

No effect of treatment was seen for mortality in the P and F1 generations. The low incidence of mortality seen in these animals was considered incidental and unrelated to treatment with TBBPA.

In the parental generations, the only effect of treatment with TBBPA was seen in the F1 males at 1000 mg/kg/day and involved lower body weights for several weekly intervals during the study and lower weight gain over the entire Week 1-11 premating period. No effect of treatment in either generation was evident from the clinical examinations, estrous cyclicity, reproductive performance, gestation/lactation body weights or food consumption, gestation length, litter data, or from the macroscopic and microscopic evaluations, organ weights, sperm evaluations, and primordial follicle counts. No effect on body weights or body weight gain was seen in the P animals or F1 parental females. Likewise, no adverse effect on food consumption was seen in the treated groups for either generation.

No effect of treatment with TBBPA was evident in the F, and F2 pups in regard to body weights, clinical findings, sex ratios, survival to weaning, macroscopic findings, or organ weight data (Day 21).

No effects on thyroid hormone levels (TSH, T3 and T4) were observed at the 10 mg/kg/day dose level in either generation. At 100 and 1000 mg/kg/day, some treatment-related effects on some thyroid hormone parameters (T3 and T4) were seen. TSH levels were unaffected, however, in either generation. Treatment with TBBPA demonstrated an increased incidence and magnitude of lower T4 values in the l00 and 1000 mg/kg/day groups. P males given 1000 mg/kg/day, and F, males given 100 or 1000 mg/kg/day also

had mild reductions in T3 values. In the absence of increases in TSH hormone levels, moderate reductions in circulating serum T4 levels, with only mild decreases in T3 for a few 1000 mg/kg/day P males, and l00 and 1000 mg/kg/day F, males, are suggestive of induction of hepatic T4-uridine diphosphate glucuronyl transferase (UDP-GT) enzymes that increase the removal of thyroxine. TBBPA has been shown in vitro to competitively displace T4 from human transthyretin, a serum carrier protein. The decreases in T4 and T3 observed in this study did not exceed the threshold for stimulation of TSH production. Thus, repeat daily dosing with TBBP A at doses of l00 or 1000 mg/kg/day to P and F1 generation rats resulted in effects on thyroid function, probably secondary to enzyme induction, without alteration in TSH activity. The 10 mg/kg/day dose was determined to be a no observed effect level (NOEL) for TBBPA and its response on thyroid function.

In the DNT/NP component, no effects of treatment were seen in F2 pups with respect to: PND 60 brain weights, PND 60 perfusion and neuropathology, special detailed clinical examinations (PND 4, 11, 21, 35, 45, and 60), motor activity (PND 13, 17, 21, and 60), auditory startle habituation (PND 22 and 60), and learning and memory (PND 22, 60 and 110). The only suggestion of a treatment-related effect was a reduction in the thickness of the parietal cortex of Day 11 pups at the 1000 mg/kg/day dose level, but not in pups at this dose level on Day 60. This change on Day 11 was not accompanied by any histologic changes in the parietal cortex, such as degeneration, necrosis, cell loss, demyelination, proliferative changes, or changes in neuronal cell density. A likely explanation for the decreased thickness of parietal cortex would be a decreased number of cells without changes in cell density. The brain weights of the 11-day-old rats were virtually equal across groups. However, it is possible that other regions of the brain were enlarged and compensated for the decrease in the thickness of parietal cortex in the affected groups. The thickness of the parietal cortex for the animals at the 10 and l00 mg/kg/day dose levels was comparable to the control. No microscopic alterations were observed in brain, spinal cord, nerves, and ganglia in the 60-day-old rats. Therefore, this apparent test-article related effect in the Day 11 F2 pup brains must be interpreted with caution, given the limitations of morphometric analysis. No effect of treatment was evident from the other parameters evaluated in the DNT/NP component. This would include the special detailed clinical observations, developmental maturation landmarks (vaginal opening and preputial separation), neurobehavioral evaluations (motor activity, learning and memory, auditory startle habituation), or Day 60 brain weights or parietal cortex thickness.

Thus, in this 2-generation reproduction study with TBBPA the No Observed Effect Level (NOEL) for parental toxicity was 100 mg/kg/day based on lower body weights and body weight gain in males at the 1000 mg/kg/day dose level. The NOEL for effects of TBBPA on thyroid hormone levels was 10 mg/kg/day based on lower T3 and T4 levels at the l00 and mg/kg/day dose levels. TSH levels, however, were not affected at any of the dose levels in either generation. The NOEL for reproductive performance and pup toxicity was 1000 mg/kg/day, the highest dose level evaluated. In the DNT/NP component, the NOEL was l00 mg/kg/day based on subtle morphometric changes in the parietal cortex in the brains of the Day 11 F2 pups, but not Day 60 F2 pups, in the 1000 mg/kg/day group. In this component no changes at any dose level were seen in the pups at any time point from clinical findings, sexual maturation landmarks, growth, or from the various behavioral

assessments. (Schroeder R. 2002. An oral two generation reproductive, fertility, and developmental neurobehavioral study of tetrabromobisphenol A in rats. Study ID Number: 474-004. MPI Research, Inc. Mattawan, MI.)

Schroeder R. 2002. An oral two generation reproductive, fertility, and developmental neurobehavioral study of tetrabromobisphenol A in rats. Study ID Number: 474-004. MPI Research, Inc. Mattawan, MI.

Effect on Fertility

Several developmental toxicity studies on TBBPA are available, one of which was recently completed under current guidelines and Good Laboratory Practices using the TBBPA in commercial production and use at a top dose of 1,000 mg/kg/d. All studies are negative for developmental toxicity.

Several repeated dose studies, in more than one mammalian species, are also available and none show evidence of an effect on the reproductive tract. According to the SIDS Manual, when teratology and 90 day studies show no effects on the reproductive system then the requirement for the reproductive endpoint are met.

In addition, a rat two-generation reproduction study found a no effect level (NOEL) of 1000 mg/kg/d for reproductive performance and pup toxicity.

Thus, the weight of the evidence indicates TBBPA does not affect fertility or reproduction

Schroeder R. 2002. An oral two generation reproductive, fertility, and developmental neurobehavioral study of tetrabromobisphenol A in rats. Study ID Number: 474-004. MPI Research, Inc. Mattawan, MI.

Schroeder, R. 2001. An oral prenatal developmental toxicity study with tetrabromobisphenol A in rats. Study No. 474-005. MPI Research, Mattawan, MI.

Schroeder R. 2002. A 90-day oral toxicity study of tetrabromobisphenol A in rats with a recovery group. Study Number: 474-006. MPI Research, Inc. Mattawan, MI.

Toxicity, Fish Chronic

Fish Early Life Stage Test

This study was sponsored by the Brominated Flame Retardant Industry Panel (BFRIP).

In an early life stage test, fathead minnow embryos and larvae were continuously exposed for 35 days to TBBPA concentrations 0, 0.024, 0.04, 0.084, 0.16 or 0.31 mg/L. The water's pH ranged from 7.0 to 8.2 over the course of the study.

Survival of embryos to doses less than 0.31 mg/L was unaffected; survival at 0.31 mg/L was less than controls.

Growth was not affected at any dose level.

The NOEC for survival and growth was 0.16 mg/L. The Maximum Acceptable Toxicant Concentration (MATC), the range encompassing the highest test concentration that had no significant effect and the lowest concentration that had a significant effect, was 0.22 mg/L for fathead minnow embryos and larvae exposed continuously for 35 days. (Surprenant 1989).

Surprenant D. 1989. The toxicity of tetrabromobisphenol A (TBBPA) to fathead minnow (Pimephales promelas) embryos and larvae. SLS Study No. 89-2-2937. Springborn Life Sciences. Wareham, Massachusettes.

WHO 1995. Tetrabromobisphenol A and Derivative. World Health Organization International Programme on Chemical Safety Environmental Health Criteria Document Number 172. Geneva.

Daphnia 21 Day Life Cycle Test

This study was sponsored by the Brominated Flame Retardant Industry Panel (BFRIP).

In a chronic study on an aquatic invertebrate species, Daphnia magna, were continuously exposed (flow-through) for 21 days to mean measured concentrations of 0.056, 0.1, 0.19, 0.30, and 0.98 mg 14C-TBBPA/L. Nominal concentrations were 0.31, 0.25, 0.5, 1.0, 2.0 mg/L. The water's pH ranged from 8.1 to 8.2 over the course of the study.

After 21 days, daphnia survival ranged from 95-100% in all treatment groups and was statistically comparable to control survival.

Organism growth, e.g. individual body length, in the all treatment groups was also comparable to the control means and was not affected by treatment at any dose level.

Reproduction at the highest dose level (0.98 mg/L measured or 2 mg/L nominal) was approximately one-third of that in the control groups and was statistically significantly different from controls. Reproduction at all other dose levels was statistically comparable to controls. The NOEC for survival was 0.98 mg/L, and the NOEC for reproduction was 0.3 mg/L.

The maximum acceptable toxicant concentration (MATC) for reproduction was > 0.3 and < 0.98 mg/L (measured concentration) or > 1 and < 2 mg/L (nominal concentration).

The MATC for survival and growth was > 0.98 mg/L (measured) or > 2 mg/L (nominal). Survival and growth were not affected by chronic exposure of Daphnia to TBBPA (Surprenant 1989).

Surprenant D. 1989. The chronic toxicity of tetrabromobsiphenol A (TBBPA) to Daphnia magna under flow-through conditions. SLS Study No. 89-01-2925. Springborn Life Sciences. Wareham, Massachusettes.

WHO 1995. Tetrabromobisphenol A and Derivative. World Health Organization International Programme on Chemical Safety Environmental Health Criteria Document Number 172. Geneva.

Chironomus 14-Day Study

This study was sponsored by the Brominated Flame Retardant Industry Panel (BFRIP).

The subchronic effects of sediment-bound TBBPA to a representative benthic invertebrate species, the midge Chironomus tentans, were determined. The degree to which sediment organic carbon concentrations affected toxicity and bioaccumulation potential were also investigated.

The study consisted of a series of three 14-day (partial life cycle) tests. Each test was conducted with sediment containing different organic carbon levels: high (6.8% organic carbon), mid (2.7%) or low (0.25%) organic carbon content. The sediments were physically characterized as having a high sand content, 2-8% silt, and were slightly acidic (pH 5.4-5.5). The TBBPA sediment concentrations were 0, 13, 25, 50, 100 and 200 mg/kg (nominal).

The test systems achieved and maintained equilibrium between sediment and water for the duration of the tests. The highest mean interstitial water concentrations of TBBPA were measured in the nominal 200 mg/kg treatments where midges were continuously exposed to interstitial water concentrations of 0.046 mg/L (HOC), 0.045 mg/L (MOC) and 0.039 mg/L (LOC) TBBPA. TBBPA concentrations in interstitial water were unrelated to the sediment's organic carbon content, but were directly proportional to TBBPA's concentration in the sediment.

Sediment/interstitial water partitioning coefficients (Kd) were 7,349, 5,378 and 5,816, in the HOC, MOC, and LOC groups, respectively, at the highest dose tested. These Kd values indicate TBBPA preferentially partitions to sediment rather than water.

Midge survival and growth in all TBBPA-treated sediments was statistically comparable to control organisms. The NOECs were 228 to 341 mg TBBPA/kg sediment, corresponding to 0.039 to 0.046 mg TBBPA/L interstitial water (Breteler 1989; WHO 1995).

Breteler R. 1989. The subchronic toxicity of sediment-sorbed tetrabromobisphenol A in the sediment midge (Chironomus tentans) under flow-through conditions. SLS No. 89-08-3067. Springborn Laboratories, Inc. Wareham, Massachusetts.

WHO 1995. Tetrabromobisphenol A and Derivative. World Health Organization International Programme on Chemical Safety Environmental Health Criteria Document Number 172. Geneva.

I U C L I D

Data Set

Existing Chemical	:	ID: 79-94-7
CAS No.	:	79-94-7
EINECS Name	:	2,2',6,6'-tetrabromo-4,4'-isopropylidenediphenol
EC No.	:	201-236-9
TSCA Name	:	Phenol, 4,4'-(1-methylethylidene)bis[2,6-dibromo-
Molecular Formula	:	C15H12Br4O2

Producer related part

Company	:	ALBEMARLE CORPORATION
Creation date	:	01.04.2005

Substance related part

Company	:	ALBEMARLE CORPORATION
Creation date	:	01.04.2005
Status	:	
Memo	:	
Printing date	:	12.08.2005
Revision date	:	
Date of last update	:	12.08.2005
Number of pages	:	72
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	
Name	:	Albemarle Corporation
Contact person	:	Marcia Hardy, DVM, PhD
Date	:	01.04.2005
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Cedex	:	
Email	:	marcia_hardy@albemarle.com
Homepage	:	
Attached document	:	This IUCLID dataset was prepared by Albemarle Corporation on behalf of and in conjuction with Great Lakes Chemical Corporation and Dead Sea Bromine Group. All three companies manufacture TBBPA.
Reliability	:	(1) valid without restriction

12.08.2005

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	
Smiles Code	:	c1c(Br)c(O)c(Br)cc1C(C)(C)c2cc(Br)c(O)c(Br)c2
Molecular formula	:	C15 H12 Br4 O2
Molecular weight	:	543.88
Petrol class	:	
Reliability	:	(1) valid without restriction

08.08.2005

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	typical for marketed substance
Substance type	:	organic
Physical status	:	solid
Purity	:	>= 98 % w/w
Colour	:	
Odour	:	
Attached document	:	TBBPA, a solid at room temperature, is a brominated phenolic molecule with a molecular weight of 543.87. The composition of the commercial product is typically >=98% TBBPA with the remainder composed of other

brominated bisphenol A compounds (primarily tribromobisphenol A). Its measured vapor pressure and log octanol/water partition coefficient are <1.19 x 10-5 Pa (Lezotte and Nixon 2001) and 8.024 (MacGregor and Nixon 2001), respectively. TBBPA's melting point is 181°C (Albemarle Corporation, 2001), and its water solubility has been described as 0.001002 mg/L (estimated, EPIWIN V3.04); <0.5 mg/L (Albemarle Corporation 2000); <0.08 mg/L (Brekelman 2000). Recently, TBBPA's water solubility was determined in unbuffered reagent water and buffered water at at pH 5, 7 and 9 using the generator column method (MacGregor and Nixon 2002). TBBPA's water solubility in non-buffered reagent water was 0.240 mg/L. TBBPA's water solubility in pH 5.0 buffer solution was 0.148 mg/L, in pH 7.0 buffer - 1.26 mg/L, and in pH 9.0 buffer - 2.34 mg/L. TBBPA's pKa was determined to be 9.40 (Ka = 3.98 x 10-10) (Lezotte And Nixon 2002).

TBBPA has been analyzed for the presence of 15 2,3,7,8-substituted polybrominated-p-dibenzodioxins and dibenzofurans. None of the analytes were present at or above the quantitation limits established by the U.S. Environmental Protection Agency (Ranken et al. 1994).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (1) (2) (3) (4) (5) (6)

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

SAYTEX BP-2000 Flame Retardant

Reliability : (1) valid without restriction
12.08.2005

TBBPA

08.08.2005

Tetrabromobisphenol A

08.08.2005

1.3 IMPURITIES

Purity : typical for marketed substance
CAS-No :
EC-No :
EINECS-Name :
Molecular formula :
Value :

Attached document : The composition of the commercial product is typically >=98% TBBPA with the remainder composed of other brominated bisphenol A compounds (primarily tribromobisphenol A).

TBBPA has been analyzed for the presence of 15 2,3,7,8-substituted polybrominated-p-dibenzodioxins and dibenzofurans. None of the analytes were present at or above the quantitation limits established by the U.S. Environmental Protection Agency (Ranken et al. 1994).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (7)

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : industrial
Category : Polymers industry

Attached document : TBBPA is used as a reactive flame retardant in epoxy resin printed circuit boards and as an additive flame retardant in acrylonitrile-butadiene-styrene (ABS) resins for electronic enclosures. In the epoxy resin circuit boards, TBBPA covalently reacts with the epoxy resin backbone and ceases to exist as a chemical entity.

TBBPA is the predominant flame retardant used in printed circuit boards worldwide. The reasons for TBBPA's dominance is that it is highly effective as a flame retardant and needs only low load levels, highly cost effective, compatible with the circuit board's other components, able to maintain the board's physical properties, qualified for industrial use, and has health and safety data supporting its use.

TBBPA is also used as the starting material for the production of TBBPA-derived flame retardants.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

Type : other: TSCA, EINECS, MITI
Additional information :

09.08.2005

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Source of exposure : other
Exposure to the : Substance

Attached document : Emissions from Flame Retarded Products

Emissions from TBBPA flame retarded end products are essentially nil. Measured TBBPA air levels from computer monitors with TBBPA-flame retarded housings were 1 ng/m3 over a 10-day period. TBBPA was not detected in air surrounding a monitor not flame retarded with TBBPA in its housing but presumably equipped with a TBBPA-flame retarded circuit board. In an office setting, TBBPA air concentrations were 0.1-2.3 ng/m3. In comparison to other semi volatiles detectable in indoor air, this level was considered very low (Ball and Herrmann 2002).

Reliability : (1) valid without restriction
12.08.2005 (8)

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

Type of search : External
Chapters covered :
Date of search : 05.08.2005

Attached document : The literature was searched using the search engine PubMed for the word

"tetrabromobisphenol A" or "79-94-7" (TBBPA's CAS Number).

Reliability : (1) valid without restriction
12.08.2005

1.13 REVIEWS

2.1 MELTING POINT

Value	:	= 181 °C
Sublimation	:	
Method	:	other
Year	:	1999
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (1)

2.2 BOILING POINT

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	< .000000119 at 20 °C
Decomposition	:	
Method	:	OECD Guide-line 104 "Vapour Pressure Curve"
Year	:	2001
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel (BFRIP). TBBPA's measured vapor pressure, using the spinning rotor gauge, is < 1.19 x 10-5 Pa (< 1.19 x 10-7 hPa).
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (9)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= 8.024 at 25 °C
pH value	:	
Method	:	other (measured)
Year	:	2001
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	This study was conducted using a composite of the commercial products

produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel (BFRIP).

TBBPA's measured log octanol/water partition coefficient, determined using the generator column method, was 8.024. Its calculated Log10 Kow was 5.903.

Reliability : (1) valid without restriction
10.08.2005 (10)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= .148 mg/l at °C
pH value	:	= 5
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	9.4 at 25 °C
Description	:	slightly soluble (0.1-100 mg/L)
Stable	:	
Deg. product	:	
Method	:	OECD Guide-line 105
Year	:	2002
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel (BFRIP).

TBBPA's water solubility has been described as 0.001002 mg/L (estimated, EPIWIN V3.04); <0.01% (Albemarle Corporation 1999) and <0.08 mg/L (Brekelmans 2000).

Recently, TBBPA's water solubility at 25 degrees C was determined in unbuffered reagent water and in buffered water at pH 5, 7 and 9 using the generator column method (MacGregor and Nixon 2002). TBBPA's water solubility in pH 5.0 buffer solution was 0.148 mg/L, in pH 7.0 buffer - 1.26 mg/L, and in pH 9.0 buffer - 2.34 mg/L. TBBPA's water solubility in non-buffered reagent water was 0.240 mg/L.

TBBPA's pKa was determined to be 9.40 (Ka = 3.98 x 10-10) (Lezotte and Nixon 2002).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (11) (12)

Solubility in	:	Water
Value	:	= 1.26 mg/l at 25 °C
pH value	:	= 7
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	9.4 at 25 °C
Description	:	slightly soluble (0.1-100 mg/L)
Stable	:	

Deg. product	:	
Method	:	OECD Guide-line 105
Year	:	2002
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel (BFRIP). TBBPA's water solubility has been described as 0.001002 mg/L (estimated, EPIWIN V3.04); <0.01% (Albemarle Corporation 1999) and <0.08 mg/L (Brekelmans 2000). Recently, TBBPA's water solubility was determined in unbuffered reagent water and in buffered water at pH 5, 7 and 9 using the generator column method (MacGregor and Nixon 2002). TBBPA's water solubility in pH 5.0 buffer solution was 0.148 mg/L, in pH 7.0 buffer - 1.26 mg/L, and in pH 9.0 buffer - 2.34 mg/L. TBBPA's water solubility in non-buffered reagent water was 0.240 mg/L. TBBPA's pKa was determined to be 9.40 (Ka = 3.98 x 10-10) (Lezotte and Nixon 2002).
Reliability	:	(2) valid with restrictions
Flag	:	Risk Assessment, Critical study for SIDS endpoint

09.08.2005 (11) (12)

Solubility in	:	other: buffered water
Value	:	= 2.34 at 25 °C
pH value	:	= 9
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	9.4 at 25 °C
Description	:	slightly soluble (0.1-100 mg/L)
Stable	:	
Deg. product	:	
Method	:	OECD Guide-line 105
Year	:	2002
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel (BFRIP). TBBPA's water solubility has been described as 0.001002 mg/L (estimated, EPIWIN V3.04); <0.01% (Albemarle Corporation 1999) and <0.08 mg/L (Brekelmans 2000). Recently, TBBPA's water solubility was determined in unbuffered reagent water and in buffered water at pH 5, 7 and 9 using the generator column method (MacGregor and Nixon 2002). TBBPA's water solubility in pH 5.0 buffer solution was 0.148 mg/L, in pH 7.0 buffer - 1.26 mg/L, and in pH 9.0 buffer - 2.34 mg/L. TBBPA's water solubility in non-buffered reagent water was 0.240 mg/L. TBBPA's pKa was determined to be 9.40 (Ka = 3.98 x 10-10) (Lezotte and

Nixon 2002).

Flag : Risk Assessment, Critical study for SIDS endpoint
09.08.2005 (11) (12)

Solubility in : other: non-buffered reagent water
Value : = .24 mg/l at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description : slightly soluble (0.1-100 mg/L)
Stable :
Deg. product :
Method : OECD Guide-line 105
Year : 2002
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel (BFRIP).

TBBPA's water solubility has been described as 0.001002 mg/L (estimated, EPIWIN V3.04); <0.01% (Albemarle Corporation 1999) and <0.08 mg/L (Brekelmans 2000).

Recently, TBBPA's water solubility was determined at pH 5, 7 and 9 using the generator column method (MacGregor and Nixon 2002). TBBPA's water solubility in pH 5.0 buffer solution was 0.148 mg/L, in pH 7.0 buffer - 1.26 mg/L, and in pH 9.0 buffer - 2.34 mg/L. TBBPA's water solubility in non-buffered reagent water was 0.240 mg/L.

TBBPA's pKa was determined to be 9.40 (Ka = 3.98 x 10-10) (Lezotte and Nixon 2002).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (11) (5)

Solubility in : Organic Solvents
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other
Year : 1999
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Attached document : TBBPA's solubility (wt. % at 25 degrees C) in the following organic solvents was reported as:
acetone.....69.60
methanol....47.20
toluene.....6.40.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint
12.08.2005 (1)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

Acid-base constant	:	pka=9.40 (ka = 3.98 x 10-10)
Method	:	
Year	:	2002
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel (BFRIP).
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

10.08.2005 (11)

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	water
Light source	:	other: fluorescent tube designed for sunbeds
Light spectrum	:	ca. 300 - 390 nm
Relative intensity	:	based on intensity of sunlight
Deg. product	:	yes
Method	:	other (measured)
Year	:	2004
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : Photolysis in Water

Eriksson et al. (2004) reported the photodegradation of TBBPA in water at various pHs (5.5-10) after UV irradiation.

The rates of decomposition were determined at a concentration of 77 uM in water. The illumination time was 50 minutes. Fluorescent tubes (Philips TL 20W/09N) provided the irradiation, and were intended to represent the range of solar UV waveleghts which penetrate the full atmosphere.

TBBPA's rate of decomposition ranged from 0.7 (pH=10) to 0.033 (pH=5.5) kx103/s. Its half-life ranged from 16 (pH=10) to 350 (pH=5.5) minutes; TBBPA's half-life at pH 7.4 = 24 minutes. The disappearance quantum yield ranged from 0.045 (pH=10) to 0.018 (pH=5.5). The quantum yield was defined as the ratio between the number of reacted molecules per unit time and unit volume and the total number of photons absorbed per unit time and unit volume.

The maximum absorption was found at 310 nm at all pH's except for pH 6.1 and 5.5 where the maximum absorbance was at 290 nm.

TBBPA decomposed via cleavage between the isopropyl group and one of the benzene rings. The main decomposition products were 4-(2-hydroxyisopropyl)-2,6-dibromophenol; 4-isopropylene-2,6-dibromophenol; and 2,6-dibromo-4-isopropylene.

The data indicated that TBBPA was readily photodegraded in aqueous solution. Degradation rates were sensitive to pH.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
12.08.2005 (13)

Type	:	water
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight

Attached document : Photolysis in Water or Silica Gel

TBBPA's calculated half-life in water by UV radiation was 10.2 days in spring, 6.6 days in summer, 25.9 days in autumn, and 80.7 days in winter. The half-life of TBBPA adsorbed onto silica gel and exposed to UV radiation was 0.12 days (reported in WHO 1995).

Flag : Critical study for SIDS endpoint
12.08.2005 (14)

Type : other: UV light plus OH radicals

Light source	:	
Light spectrum	:	> 290 nm
Relative intensity	:	based on intensity of sunlight
Deg. product	:	
Method	:	other (measured)
Year	:	1998
GLP	:	no
Test substance	:	other TS

Attached document : Photolysis of TBBPA in the presence of UV light and hydroxyl radicals has also been reported; TBBPA was reported to totally degrade within 5-6 days with an estimated 33 hour half-life (Eriksson and Jakobsson 1998).

Flag : Critical study for SIDS endpoint

12.08.2005 (15)

3.1.2 STABILITY IN WATER

3.1.3 STABILITY IN SOIL

Type	:	laboratory
Radiolabel	:	
Concentration	:	
Soil temperature	:	°C
Soil humidity	:	
Soil classification	:	
Year	:	

Attached document : Mobility in Soil

The mobility and sorption of TBBPA was studied in a Glyndon silt loam soil. The soil was contained in a glass column with a stainless steel end cap. After achieving steady-state flow velocity with CaCl2, a pulse of 14C-TBBPA (500 ppb, the upper concentration reported in Swedish sediment) was applied and eluted with additional CaCl2. The eluate was collected. The soil was extruded from the column, compressed, cut into 1 cm sections and combusted. Selected sections were analyzed using thin layer chromatography. TBBPA sorption was measured using a batch equilibrium technique and liquid scintillation counting.
TBBPA was not eluted from the soil column even after 11 pore volumes were displaced. Combustion analysis of the soil sections showed that 16.2% of 14C-activity remained in the first centimeter of soil with 6-7% in each of the next four sections. Batch studies at 48 h showed that 97.9, 92.6 and 93.6% of the 0.025, 0.25 and 2.5 um/ml 14C-TBBPA were bound to the soil. Thus, there was re-distribution of TBBPA in the soil column to a depth of 15 cm. Strong adsorption of TBBPA to soil particles prevented movement into the aqueous phase. In the environment, TBBPA would be expected to sorb largely to sediment and organic matter in soil (Larsen et al. 2001).

12.08.2005 (16)

Type	:	laboratory
Radiolabel	:	
Concentration	:	
Soil temperature	:	°C
Soil humidity	:	
Soil classification	:	
Year	:	
Deg. product	:	

Method	:	other
Year	:	1989
GLP	:	yes
Test substance	:	other TS: 14C-TBBPA
Attached document	:	64-Day Aerobic Soil Degradation

This study was performed according to Good Laboratory Practices and according to US EPA OPPTS guidelines. Sponsor: Brominated Flame Retardant Industry Panel (BFRIP).

The biodegradability of 14C-TBBPA was tested under aerobic conditions in three soil types, i.e., Massachusetts sandy loam, a California clay loam, and Arkansas silty loam. The three soil types contained: sand (83%)-silt (13%)-clay (4%), sand (16%)-silt (58%)-clay (26%), and sand (43%)-silt (24%)-clay (33%), respectively. Thin layer chromatography (TLC) showed biodegradation of TBBPA in all soil types. Less than or equal to 6% of the applied radioactive TBBPA was recovered in the volatile traps, indicating partial degradation to C02. Results of the TLC analysis indicated variable degradation rates of TBBPA which were dependent on soil type. After 64 days, the amount of TBBPA remaining in the soils ranged from 36 to 82%, with the highest level in sandy loam soil and the lowest in the silty loam soil. Degradation products (2 or 3 depending on soil type) were not specifically identified, but the dimethyl and diethyl derivatives of TBBPA were ruled out based on TLC characteristics of authentic standards (Fackler 1989).

Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (17) (14)

Type	:	laboratory
Radiolabel	:	
Concentration	:	
Soil temperature	:	°C
Soil humidity	:	
Soil classification	:	
Year	:	
Deg. product	:	
Method	:	other
Year	:	1989
GLP	:	yes
Test substance	:	other TS: 14C-TBBPA
Attached document	:	64-Day Anaerobic Soil Degradation

This study was performed according to Good Laboratory Practices and according to US EPA OPPTS guidelines. Sponsor: Brominated Flame Retardant Industry Panel (BFRIP).

The biodegradability of TBBPA was tested under anaerobic conditions in three soil types; Massachusetts sandy loam (MSL), Arkansas silty loam (ASL), and California clay loam (CCL). The three soil types contained: sand (83%)-silt (13%)-clay (4%), sand (16%)-silt (58%)-clay (26%), and sand (43%)-silt (24%)-clay (33%), respectively. Thin layer chromatography showed biodegradation of TBBPA in all soil types. Less than 0.5% of the radiolabel was recovered in the volatile traps, indicating little degradation to C02. The recovered radioactivity in all traps was almost exclusively C02. Results of the TLC analysis indicated variable degradation rates that were dependent on the soil type. After 64 days, the amount of TBBPA remaining in the soils were MSL: 43.7-57.4%, ASL: 53.4-65%, and CCL: 89.5-90.6%. Radioactivity recovered from the water ranged from 0.5 to 2.5%. Degradation products (2 or 3 depending on soil type) were not specifically

identified, but the dimethyl and diethyl derivatives of TBBPA were ruled out based on TLC characteristics of authentic standards. (Fackler 1989; WHO 1995.)

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (18) (14)

3.2.1 MONITORING DATA

Type of measurement : background concentration
Media : surface water
Concentration :
Method :

Attached document : Water

In 1977, in Japan, none of 15 water samples analyzed contained TBBPA (LOD 0.02-0.04 ug/L). Water samples were collected in 25 area in Japan in 1986-86. TBBPA was detected in one out of three water samples from teh mouth of the Yamato River (Environment Agency Japan 1989). In 1987, in Japan, TBBPA was detected in one out of 75 water samples at a concentration of 0.05 ug/L (LOD 0.03 ug/L). In 1988-89, in Japan, TBBPA was not detected in 150 water samples collected at 50 locations (LOD 0.04 ug/L) (Environment Agency Japan 1989, 1991). As cited in WHO 1995.

Reliability : (1) valid without restriction
12.08.2005 (14)

Type of measurement : background concentration
Media : sediment
Concentration :
Method :

Attached document : Sediment

Japan
TBBPA was detected at 0.5-140 ug/kg (d wt) in 14 out of 19 river sediment samples in Osaka, Japan. In marine seidments in Osaka Bay, Levels of 0.5-4.5 ug/kg (d wt) were found in 1981-83. In the marine sediments of two areas other than Osaka, the levels were much lower (n.d.-1.8 ug/kg d wt). TBBPA was reported at a concentration of approximately 20 ug/kg d wt in river seidment collected in 1981 downstream of the Neya River which empties into the Osaka Bay. As cited in the WHO 1995.

Sediment samples were collected in 22 areas, in Japan, in 1987. TBBPA was found in the bottom sediment from 6 areas; the mouth of the Sumida River (3/3), the mouth of Ara River (1/3), the mouth of the Yamato River (3/3), the river flowing in Osaka City (3/3), the Port of Osaka (3/3) and the mouth of Yodo River (1/3).

TBBPA was detected in 14 out of 66 sediment samples at concentrations ranging from 2 to 150 ug/kg d w and in 20 out of 130 sediment samples collected at 44 locations in concentrations ranging from 2 to 108 ug/kg d wt in 1988 (LOD=2 ug/kg dw).

Sweden
Sellstrom et al. (1990) also reported detection of TBBPA in sediment samples from a river in Sweden. However, the levels are reported as ug/ignition loss and are thus not informative.

UK, Belgium,The Netherlands

TBBPA was detected (9.8 mg/kg dw) in River Skerne (UK) sediment in the vicinity of a BFR manufacturing site. TBBPA was detected in lower concentrations (25 ug/kg dw) in the River Tees, to which the Skerne is a tributary. No TBBPA was detected in sediment offshore from the Tees or in sediment collected from the River Clyde, Scotland. TBBPA was detected in trace quantities in some but not all sediments collected in the Scheldt estuary and the Antwerp harbor (Morris et al. 2004).

Verslycke et al (2005) did not detect TBBPA in sediment collected from 3 sites in the Scheldt estuary.

12.08.2005 (19) (20) (14)

Type of measurement : concentration at contaminated site
Media : air
Concentration :
Method :

Attached document : Air

Zweidinger et al (1979) reported a TBBPA air concentration near a production facility in Southern Arkansas of 1.8 ug TBBPA/m3.

12.08.2005 (14)

Type of measurement : background concentration
Media : air
Concentration :
Method :

Attached document : In a study to identify the source of contamination of procedural blanks in an analytical laboratory, TBBPA was identified in some laboratory air samples at concentrations below the limit of quantification.

12.08.2005 (21)

Type of measurement : background concentration
Media : air
Concentration :
Method :

Attached document : TBBPA air concentrations were measured in air at an electronics recycling company and in other work places in Sweden (Sjodin et al. 2001). In the dismantling hall, the mean TBBPA air concentration was 30 ng/m3 with a range of 12-70 ng/m3. In the area around the plastics shreder, the TBBPA air concentration was measured as 130 or 150 ng/m3 when plastic containing a brominated flame retardants was being shredded. Air levels where circuit boards were being assembled were 0.2 ng/m3 (mean) and ranged from 0.11-0.37 ng/m3. In an office containing computers, air concentrations wer areported to be 0.036 ng/m3 (mean), ranging from 0.01-0.07 ng/m3. Measured air levels at a computer repair facility were 0.031 and 0.038 ng/m3, and in a teaching hall 0.035 and 0.15 ng/m3. TBBPA was not detected in outdoor air.

12.08.2005 (22)

Type of measurement : background concentration
Media : biota
Concentration :
Method :

Attached document : Biota

Fish and Shellfish
TBBPA was not detected in mussels (Mytilus edulis) collected in Osaka Bay in 1981 (WHO 1995).

TBBPA was not detected in 75 fish samples collected from 24 area in Japan in 1987. TBBPA was also not detected in 135 samples collected at 45 diffierent location sin Japan in 1988 (LOD=1 ug/kg ww) (WHO 1995).

TBBPA was either not detected or detected only in trace quantities in eel collected in the Scheldt estuary, The Netherlands (Verslycke et al 2005).

Aquatic Invertebrates
TBBPA was detected only in trace amounts in mysid from 2/3 inland sites in the Netherlands, and was below the limit of detection in all sediment samples collected in the Scheldt estuary (Verslycke et al 2005).

12.08.2005 (19) (20) (14)

Type of measurement : background concentration
Media : other: sewage sludge and/or effluent
Concentration :
Method :

Attached document : TBBPA was detected in UK sewage treatment influent, primarily in the dissolved phase, at a range of 2.6 - 85 ng/L. A maximum concentration of of 192 ug/kg was dtected in a secondary treated and dewatered sludge sample from Cork, Ireland. TBBPA was detected in Dutch sewage treatment plant effluent at 3-63 ug/kg dw, and in sludge at a manimum of 600 ug/kg dw (Morris et al 2004).

Leachate from 3 UK landfills showed no evidence of TBBPA. TBBPA was reported at a median value of < 25 ug/kg in Dutch leachate (Morris et al 2004).

12.08.2005 (19)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III
Media :
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method :
Year :

Attached document : TBBPA is predicted to partition to soil and sediment if released to the environment. Based on a release of 1,000 kg/hr to air, water and soil, the predicted partitioning is: air - 0.0000004%, water - 1.13%, soil - 44.9%, and sediment - 53.9% (Level III Fugacity Model, EPIWIN V3.04, Syracuse Research Corporation). The majority would be reacted in sediment and soil (83.9%) with only 16.1% of the total able to undergo advection. TBBPA is expected to be essentially immobile in soil, where it can undergo degradation.

TBBPA is not expected to volatilize from water based on its estimated air-water partition coefficient (9.4 x 10-12) and river and lake volatilization half lives (river: 6.7 x 10+5 years; lake: 7.3 x 10+6 years). TBBPA would be expected to partition to biomass from water based on its estimated partition

coefficient (3.1 x 10+6). All estimates were made using EPIWIN V3.04 (Syracuse Research Corporation).

While not expected to undergo biodegradation during sewage treatment, TBBPA is expected to be removed from the effluent during passage through a wastewater treatment plant. Removal is estimated to be via sludge adsorption (93.14%) with only minimal biodegradation (0.78%). A total removal of 93.9% is predicted (STP Fugacity Model, EPIWIN V3.04, Syracuse Research Corporation).

12.08.2005

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge, adapted
Concentration	:	100 mg/l related to Test substance 30 mg/l related to
Contact time	:	14 day(s)
Degradation	:	= 0 (±) % after 14 day(s)
Result	:	under test conditions no biodegradation observed
Deg. product	:	
Method	:	other: MITI
Year	:	1992
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	TBBPA was tested in Japan's activated sludge biodegradation test. The concentraton of sludge in the system was 30 mg/L. No biodegradation was observed over the 14-day study (CITI 1992). The nonbrominated analog of TBBPA also exhibited no degradation under these conditions.
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (23)

Type	:	aerobic
Inoculum	:	other: natural river sediment and water
Contact time	:	56 day(s)
Degradation	:	(±) % after
Result	:	inherently biodegradable
Deg. product	:	
Method	:	other
Year	:	1989
GLP	:	yes
Test substance	:	other TS: 14C-TBBPA
Attached document	:	56-Day Sediment/Water Microbial Degradation

This study was sponsored by the Brominated Flame Retardant Industry Panel (BFRIP).

The biodegradability of 14C-TBBPA was tested under aerobic conditions in a sediment/water microbial test system using natural river sediment and water. The test conditions were pH 5.5, field moisture capacity 15.9%,

temperature 24-26 degrees C, and the composition of the soil (6.8% carbon) was 925 sand, 6% silt, and 2% clay.

TBBPA biodegraded at all tested concentrations (0.01, 0.1 and 1 mg/L). Half-lives calculated for TBBPA in the sediment/water microbial test systems ranged between 48 days at 0.01 ug/L concentration and 84 days at the 1 mg/L concentration with apparent correlations between half-life and TBBPA concentration and half-life and microbial population. The half-life in sterile sediment was extrapolated to be 1300 days, indicating that the degradation observed in the active test systems was due to microbial degradation rather than physical processes.

Less than 8% of the applied radioactive carbon from TBBPA was recovered in the volatile traps indicating partial degradation to C02.

Filtered water contained less than 5% of the applied radioactivity.

The amount of radioactivity observed to be remaining in the sediment at test termination, 44.7, 64.2, and 60.8% in the 0.01, 0.1 and 1 mg radioactive TBBPA/L treatments, respectively, was comparable to the amounts reported in the aerobic degradation study in soil.

Half-lives calculated for TBBPA in the sediment/water microbial test systems ranged between 48 and 84 days, with an apparent correlation between half-life and concentration of TBBPA and half-life and microbial population. (Fackler 1989; WHO 1995.)

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (24) (14)

Type : anaerobic
Inoculum : other: estuarine sediment
Contact time : 120 day(s)
Degradation : (±) % after
Result : inherently biodegradable
Deg. product : yes
Method : other
Year : 2002
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Attached document : Anaerobic Biotransformation in Estuarine Sediments

Degradation of TBBPA was studied in anoxic estuarine sediments under methanogenic or sufate-reducing conditions. Sediment grab samples were collected from the Arthur KIll tidal strait located between Staten Island and New Jersey, U.S. Anaerobic enrichments used in the test contained 25% v/v live Arthur Kill sediment. The nominal concentration of TBBPA tested in the enrichments was 225-275 uM. Greater than 95% of the TBBPA partitioned to the sediment.

Under methanogenic conditions, initial TBBPA loss was observed within 14 days with a nearly concomitant stoichiometrically equivalent amount of bisphenol A (BPA) produced. Near complete loss of TBBPA was seen within 55 days. Based on Fig 1, TBBPA's half-life is estimated to be approximately 28 days.

Under sulfate-reducing conditions, degradation of TBBPA commenced after a lag period of 28 days and was virtually complete within 112 days. BPA was not detected until after there had been substantial loss of TBBPA (after 70 days). Based on Fig 1, TBBPA's half-life is estimated to be approximately 40 days.

No loss of TBBPA was observed in the autoclaved controls.

Under methanogenic and sulfidogenic conditions, complete dehalogenation of TBBPA to BPA, with no further degradation of BPA, was observed. Dehalogenation of TBBPA to BPA was much slower in the sulfate-reducing enrichments than in the methanogenic enrichments. TBBPA's half-life is estimated to be 28 (methanogenic) and 40 (sufidogenic) days (Voordeckers et al 2002).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (25)

Deg. product :
Method : other
Year : 2000
GLP : no data
Test substance :

Attached document : Sequential Anaerobic-Aerobic Microbial Degradation

The degradation of TBBPA was evaluated in a sequential anaerobic-aerobic system. TBBPA was incubated with a slurry of anaerobic sediment from a wet ephemeral desert stream bed contaminated with chemical industry waste. Anaerobic incubation resulted in an 80% decreased in the original TBBPA concentration. One metabolite was produced and identified as bisphenol A (BPA). BPA persisted in the anaerobic slurry but was degraded aerobically by gram negative bacteria present in the contaminated soil. Thus, sequential anaerobic-aerobic degradation of TBBPA was observed (Ronen et al. 2000). In a letter report to the UK Environment Agency, the authors later reported they were unable to repeat the results.

Reliability : (4) not assignable
12.08.2005 (26)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species : Cyprinus carpio (Fish, fresh water)
Exposure period : 56 day(s) at °C
Concentration :
BCF : ca. 30 - 485
Elimination :
Method : other: MITI
Year : 1992
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Attached document : BCF in Japanese Carp

The bioconcentration of TBBPA was evaluated in Japanese carp following an 8 week exposure period at concentrations of 8 or 80 ug/L. The BCF was 30-341 at 80 ug/L and 52-485 at 8 ug/L. The LC50 in killifish was determined to be 8.2 mg/L at 48 hours (CITI 1992; reported in WHO 1995).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (27) (14)

Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	24 day(s) at °C
Concentration	:	4.7 µg/l
BCF	:	= 307
Elimination	:	yes
Method	:	other
Year	:	1989
GLP	:	yes
Test substance	:	other TS:14C-TBBPA

Attached document : Fathead Minnow Bioconcentration Study using 14C-TBBPA

This study was sponsored by the Brominated Flame Retardant Industry Panel (BFRIP).

Fathead minnows were exposed to 4.7 ug/L 14C-TBBPA (flow through conditions) for a 24-day exposure period followed by a 6-day depuration period. 14C-activity remained below the limit of radiometric detection in water during depuration. The concentration of 14C-activity in fish tissue reached a steady-state level on day 4 of exposure. The BCF of the parent compound (TBBPA) was 307. Appendix 1 (pages 36-40) of the amended final report of the fathead minnow study reveals that only 24.9% (15.2% carcass + 9.7% viscera) of the total recovered 14C-activity in the fish was associated with TBBPA. The remainder was associated with metabolites. The fish whole body tissue concentration was calculated as 5,800 ug/kg based on total 14C-activity. Of this 5,800 ug/kg, 24.9% or 1,444.2 ug/kg were associated with TBBPA based on the TLC results. Thus, a mean water concentration of 4.7 ug/L, the fish BCF for TBBPA is 307. TBBPA's BCF was previously reported in error to be 1200, based on total 14C-activity.

The results of this study indicated ready uptake in continuously exposed fathead minnows with steady-state reached within 4 days. Extending the period of continuous exposure up to 24 days did not increase the levels in fish. During depuration, the fathead minnows rapidly and nearly completely eliminated the 14C-residue. The whole body half- life was < 24 hours and by day 6 of the elimination period only 2% of the 14C-residue remained in the exposed fish. Therefore, these residues should not persist once the fish are no longer continuously exposed. Intermittent exposures should not result in any significant TBBPA tissue residues because of the short half-life (<24 hours) of TBBPA and its metabolites.

TBBPA's fish BCF was 307. Rapid elimination of the radiolabel was observed. The whole-body half-life in the fish was < 1 day. 98% of the 14C-activity was eliminated by 6 days of depuration; elimination of 95% occurred between day 1 and 4 of depuration. 14C-TBBPA residues did not persist in fish tissue (Fackler 1989; WHO 1995).

Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (28) (14)

Species	:	Lepomis macrochirus (Fish, fresh water)
Exposure period	:	28 day(s) at °C
Concentration	:	.0098 mg/l
Elimination	:	yes
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	other TS: 14C-TBBPA

Attached document	:	Bluegill Sunfish Bioconcentration Study using 14C-TBBPA

Blue gill sunfish were exposed to 14C-TBBPA for 28 days to 0.0098 mg/L (flow-through) followed by a 14-day withdrawal period. The bioconcentration factor (BCF) in edible tissue was 20 and 170 in visceral tissue. These BCF values were based on 14C-residues and therefore represent the sum total of parent compound, any retained metabolites and assimilated carbon. Plateau levels were reached within 3-7 days. The whole body half-life was < 24 hours. The radiocarbon dissipation to <0.01 mg/kg in fish tissue occurred within 3-7 days of the beginning of the withdrawal phase. TBBPA did not show accumulation potential in this test. (Nye, D., 1978, Project 780241; reported in Environmental Health Criteria Document # 172, World Health Organization, Geneva, 1995)

Reliability	:	(2) valid with restrictions
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (29) (14)

Species	:	other: Eastern oyster
Exposure period	:	20 day(s) at °C
Concentration	:	
BCF	:	= 148
Elimination	:	yes
Method	:	other
Year	:	1989
GLP	:	yes
Test substance	:	other TS: 14C-TBBPA

Attached document	:	Bioconcentration Study in Eastern Oysters

This study was sponsored by the Brominated Flame Retardant Industry Panel (BFRIP).

Eastern oysters were exposed to nominal concentration of 1 ug/L of 14C-TBBPA for 20 D followed by a 14-day depuration period. The concentration of 14C-residues in the aquaria water remained constant throughout the 20-day exposure period. During depuration 14C-residues in the water remained < 0.34 ug/L, the limit of radiometric detection. 14C-residues reached steady-state in oyster tissues by day 5.

Appendix 1 (pages 36-39) of the amended final report of the oyster study shows that only 20.6% of total 14C-activity in the oysters was associated with TBBPA. The remainder was associated with metabolites. The mean steady state concentration, based on total 14C-residues, was 720 ug/kg. Of this 720 ug/kg, 148.3 ug/kg were associated with TBBPA based on the TLC results. At a mean water concentration of 1.0 ug/L, TBBPA's mean steady-state BCF in the oyster was 148. The depuration half-life was between 3-5 days (Fackler 1989; WHO 1995).

Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (30) (14)

Species	:	other: Chironmus
Exposure period	:	14 day(s) at °C
Concentration	:	
Elimination	:	
Method	:	other
Year	:	1989
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Attached document	:	Sediment Midge

This study was sponsored by the Brominated Flame Retardant Industry Panel.

The subchronic effects of TBBPA on the survival and growth of the sediment midge, Chironomus tentans, were evaluated in a 14 day continuous exposure via treated sediments under flow-through conditions. As a part of the study, bioconcentration factors were calculated as the ratio of the body and interstitial water concentrations. In the high (6.8%) organic carbon sediment, the BCFs ranged from 243-511 over the 5 dose levels. In the mid (2.7%) organic carbon sediment, the BCFs ranged from 487-1140. In the low (0.25%) organic carbon sediment, the BCFs ranged from 646 to 3190.

Bioconcentration appeared a function of the interstitial water concentrations, which were in turn a function of the sediment bound TBBPA concentrations and sediment organic carbon content. Bioavailability appeared to be affected by the total organic carbon content in the sediment due to the increase observed at the lowest organic carbon content (0.25%). In the high and mid organic carbon sediments, TBBPA's BCF was ~ 1,000, and appeared independent of exposure concentrations. Only in the low (<1%) organic carbon sediment at the highest dose tested, 200 mg/kg sediment, was the BCF > 1,500. No adverse effects occurred in the organisms (Breteler 1989; WHO 1995).

Reliability : (2) valid with restrictions
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (31) (14)

3.8 ADDITIONAL REMARKS

Memo : Discussion: Potential for Environmental Degradation and Bioaccumulation

Attached document : Laboratory studies indicate TBBPA is potentially degradable in the environment (Sections 3.1, 3.5), and therefore not peristent. Aerobic and anaerobic studies indicate a soil half-life of approximately 50 days. An aerobic sediment/water degradation study produced a half-life of approximately 67 days, and half-lives of 28 and 40 days were estimated from an anaerobic sediment study. TBBPA also appears rapidly photodegradable in water, with half lives ranging from 16-360 minutes depending on pH.

Laboratory studies also indicate TBBPA has little potential to bioaccumulate (Section 3.7). With two hydroxyl groups, TBBPA is readily metabolized to more water soluble conjugates and rapidly eliminated.

Reliability : (1) valid without restriction
12.08.2005

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Attached document : The 96-hour LC50 values for bluegill sunfish (Calmbacher 1978), rainbow trout (Calmbacher 1978) and fathead minnow (pH=8.6-9.6) (Surprenant 1988; sponsored by the Brominated Flame Retardant Industry Panel) were 0.51, 0.40 and 0.54 mg/L, respectively.

The LC50 in killifish was determined to be 8.2 mg/L at 48 hours (CITI 1992).

These acute studies were reported in WHO 1995.

Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (32) (27) (33) (14)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Attached document : The 48-hour LC50 for Daphnia magna was 0.96 mg/L (Morrissey 1978).

The 96 hour EC50 for the Eastern oyster was 0.098 mg/L (pH=7.9-8.1) (Surprenant 1989; Sponsored by the Brominated Flame Retardant Industry Panel).

The 96 hour EC50 in <1, 5, or 10 day old Mysid shrimp was 0.86, 1.1, and 1.2 mg/L, respectively (Goodman et al. 1988) .

These acute studies were reported in WHO 1995.

Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (34) (35) (36) (14)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Attached document : The growth of freshwater green algae, Selenastum capricornutum, was not affected by 5.6 mg/L, the highest level tested (pH=8.6-9.6) (Giddings 1988).

The growth of marine unicellular alga, Skeletonema costatum, Thalassiosira pseudonana, and Chlorella sp. in six different marine media was investigated following TBBPA exposure. The 96 hr EC50 for Clorella was > 1.5 mg/L, the highest dose tested. The 72 hr EC50 for S. costatum ranged from 0.09-1.14 mg/L. The 72 hr EC50 for T. pseudonana ranged from 0.13-1.0 mg/L (Walsh et al. 1987).

These studies were reported in WHO 1995.

Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (37) (38) (14)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

Species	:	Pimephales promelas (Fish, fresh water)
Endpoint	:	other: survival and growth
Exposure period	:	35 day(s)
Unit	:	mg/l
NOEC	:	= .16 measured/nominal
Method	:	other
Year	:	1989
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : Fish Early Life Stage Test

This study was sponsored by the Brominated Flame Retardant Industry Panel (BFRIP).

In an early life stage test, fathead minnow embryos and larvae were continuously exposed for 35 days to TBBPA concentrations 0, 0.024, 0.04, 0.084, 0.16 or 0.31 mg/L. The water's pH ranged from 7.0 to 8.2 over the course of the study.

Survival of embryos to doses less than 0.31 mg/L was unaffected; survival at 0.31 mg/L was less than controls.
Growth was not affected at any dose level.

The NOEC for survival and growth was 0.16 mg/L. The Maximum Acceptable Toxicant Concentration (MATC), the range encompassing the highest test concentration that had no significant effect and the lowest concentration that had a significant effect, was 0.22 mg/L for fathead minnow embryos and larvae exposed continuously for 35 days. (Surprenant 1989).

Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (39) (14)

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species	:	Daphnia magna (Crustacea)
Endpoint	:	other: survival, growth, reproduction
Exposure period	:	21 day(s)
Unit	:	
Analytical monitoring	:	yes
Method	:	other
Year	:	1989
GLP	:	yes
Test substance	:	other TS: 14C-TBBPA

Attached document : Daphnia 21 Day Life Cycle Test

This study was sponsored by the Brominated Flame Retardant Industry Panel (BFRIP).

In a chronic study on an aquatic invertebrate specie, Daphnia magna, were continuously exposed (flow-through) for 21 days to mean measured concentrations of 0.056, 0.1, 0.19, 0.30, and 0.98 mg 14C-TBBPA/L. Nominal concentrations were 0.31, 0.25, 0.5, 1.0, 2.0 mg/L. The water's pH ranged from 8.1 to 8.2 over the course of the study.

After 21 days, daphnia survival ranged from 95-100% in all treatment groups and was statistically comparable to control survival.

Organism growth, e.g. individual body length, in the all treatment groups was also comparable to the control means and was not affected by treatment at any dose level.

Reproduction at the highest dose level (0.98 mg/L measured or 2 mg/L nominal) was approximately one-third of that in the control groups and was statistically significantly different from controls. Reproduction at all other dose levels was statistically comparable to controls. The NOEC for survival was 0.98 mg/L, and the NOEC for reproduction was 0.3 mg/L.

The maximum acceptable toxicant concentration (MATC) for reproduction was > 0.3 and < 0.98 mg/L (measured concentration) or > 1 and < 2 mg/L (nominal concentration).

The MATC for survival and growth was > 0.98 mg/L (measured) or > 2 mg/L (nominal). Survival and growth were not affected by chronic exposure of Daphnia to TBBPA
(Surprenant 1989).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (40) (14)

Species : other aquatic mollusc: Mytilus edulis
Endpoint : other: growth
Exposure period : 70 day(s)
Unit : µg/l
NOEC : = 17 measured/nominal
Analytical monitoring : yes
Method : other
Year : 2005
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : Blue Mussel 70-Day Flow-Through Study

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel (BFRIP)

The effect of TBBPA on the growth of the common marine blue mussel (Mytilus edulis) was determined in a 70-day flow-through study without aeration. Test groups consisted of a dilution water control, solvent control and nominal TBBPA concentrations of 19, 38, 75, 150 and 300 ug/L. Mean measured concentrations over the exposure duration were <2.5, <2.5, 17, 32, 62, 126 and 226 ug/L. The highest nominal concentration was the maximum solubility of the test substance in the flow through system.

The test was conducted in triplicates. On day 0, 10 mussels were randomly selected from a pooled population, individual shell lengths measured, and randomly placed in the replicate test tanks. Shell lengths of 30 additional mussels were determined, the mussels sacrificed, and the wet and dry flesh weights determined. Every 14 days the mussels on-test were measured. The exposure was terminated after 70 days when the dilution water control mussels had achieved a mean increase in shell length > 50% of their shell length on day 0. On day 70 all mussels were removed from the tanks, their shells measured and the wet and dry mussel flesh weights determined.

The pH of the replicate tanks ranged from 7.9 to 8.1 throughout the test. The dissolved oxygen concentrations ranged from 7.2 to 8.2 mg/L. The

temperature range was 15 ± 1 °C.

The specific growth rates (SGR) of mussels were analyzed using procedures outline in the OECD method 215 Fish, Juvenile Growth Test. For each individual mussel, the SGR length or weight per day was calculated based on both shell length nd body weight data. The SGR was calculated based on shell length data on days 0-14, 0-28, 0-42, 0-56 and 0-70, and based on tissue wet and dry weight data on days 0-70.

For SGR(shell length), days 0-70, the LOEC (p=0.05) was 32 ug/L and the NOEC (p=0.05) was 17 ug/L. For SGT(wet weight), the LOEC (p=0.05) was 126 ug/L and the NOEC (p=0.05) was 62 ug/L. For SGT(dry weight), the LOEC (p=0.05) was 32 ug/L and the NOEC (p=0.05) was 17 ug/L. The overall NOEC based on both SGRs for days 0-70 was 17 ug/L (Brown R et al. 2005).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (41)

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

Species : Chironomus
Endpoint : other: survival and growth
Exposure period : 14 other:days
Unit :
Method :
Year : 1989
GLP :
Test substance : as prescribed by 1.1 - 1.4

Attached document : Chironmus 14-Day Study

This study was sponsored by the Brominated Flame Retardant Industry Panel (BFRIP).

The subchronic effects of sediment-bound TBBPA to a representative benthic invertebrate species, the midge Chironomus tentans, were determined. The degree to which sediment organic carbon concentrations affected toxicity and bioaccumlation potential were also investigated.

The study consisted of a series of three 14-day (partial life cycle) tests. Each test was conducted with sediment containing different organic carbon levels: high (6.8% organic carbon), mid (2.7%) or low (0.25%) organic carbon content. The sediments were physically characterized as having a high sand content, 2-8% silt, and were slightly acidic (pH 5.4-5.5). The TBBPA sediment concentrations were 0, 13, 25, 50, 100 and 200 mg/kg (nominal).

The test systems achieved and maintained equilibrium between sediment and water for the duration of the tests. The highest mean interstitial water concentrations of TBBPA were measured in the nominal 200 mg/kg treatments where midges were continuously exposed to interstitial water concentrations of 0.046 mg/L (HOC), 0.045 mg/L (MOC) and 0.039 mg/L (LOC) TBBPA. TBBPA concentrations in interstitial water were unrelated to the sediment's organic carbon content, but were directly proportional to TBBPA's concentration in the sediment.

Sediment/interstitial water partitioning coefficients (Kd) were 7,349, 5,378 and 5,816, in the HOC, MOC, and LOC groups, respectively, at the highest dose tested. These Kd values indicate TBBPA preferentially partitions to

sediment rather than water.

Midge survival and growth in all TBBPA-treated sediments was statistically comparable to control organisms. The NOECs were 228 to 341 mg TBBPA/kg sediment, corresponding to 0.039 to 0.046 mg TBBPA/L interstitial water (Breteler 1989; WHO 1995).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (42) (14)

Species : Lumbriculus
Endpoint : other: survival and growth
Exposure period : 28 other:days
Unit : mg/kg sediment dw
NOEC : = 254 measured/nominal
LC50 : = 405 measured/nominal
LOEC : = 426 measured/nominal
Method : ASTM E1706-95b sediment toxicity test
Year : 2002
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : Sediment Organism Toxicity, 5% TOC

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and ASTM guidelines.

The objective of this study was to determine the effects of sediment-incorporated TBBPA, on the oligochaete, Lumbriculus variegates during a 28-day exposure period under flow-through test conditions using sediment with 5% total organic carbon content. The measured endpoints of the test were survivorship (original organisms and/or offspring) and growth as determined by dry weight measurements.

Groups of oligochaetes were exposed to a geometric series of six test concentrations and a negative control (untreated sediment) for 28 days under flow-through test conditions. Eight replicate test compartments were maintained for biological observations in each treatment and control group, with 10 oligochaetes in each test compartment, for a total of 80 oligochaetes per test concentration. Each test compartment contained a quantity of sediment and overlying water. Additional replicates were added in each treatment and control group for analytical sampling of water and sediment. The "analytical" replicates sampled on Day 0 contained no oligochaetes, while oligochaetes were added at test initiation to the "analytical" replicates sampled on Day 7 and at test termination. Nominal test concentrations selected in consultation with the sponsor were 90, 151, 254, 426, 715 and 1200 mg/Kg of sediment based on the dry weight of the sediment. The results of the study are based on the Day 0 nominal test concentrations. Overlying water, pore water and sediment samples were collected and analyzed from the "analytical replicates" of the control group and the lowest and two highest test concentrations. The collection and analysis were done approximately one-half hour after the addition of test organisms to the test system on Day 0, on Day 7 and at the end of the test. Results of the analyses were used to confirm the lowest and two highest test concentrations. Test compartments were impartially positioned in a diluter unit approximately 48 hours prior to test initiation to condition the sediment prior to introduction of organisms. Oligochaetes were impartially assigned to exposure compartments at test initiation. Observations of mortality and abnormal behavior were made at least three times per week

during the test. Survivorship/reproduction and growth (dry weights) were determined at the end of the 28-day test period. The percent reduction in the numbers of organisms present in the treatment groups at test termination in comparison to the control group was used to determine the 28-day EC50 value. The lowest-observed-effect-concentration (LOEC) and the no-observed-effect-concentration (NOEC) were determined by the concentration-response pattern and statistical analysis of the survival/reproduction and dry weight data.

The 28-day EC50 value for oligochaetes (Lumbriculus variegatus) exposed to TBBPA in sediment was 405 mg/Kg dry weight of sediment based on survival/reproduction. The lowest-observed-effect-concentration (LOEC) and the no-observed-effect-concentration (NOEC) were based on the survival/reproduction and dry weight data. The survival/reproduction data and the dry weight data were both sensitive parameters in this study. Based on the results of this study, the LOEC was 426 mg/Kg dry weight of sediment and the NOEC was 254 mg/Kg dry weight of sediment. (Krueger et al. 2002)

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (43)

Species : Lumbriculus
Endpoint : other: survival and growth
Exposure period : 28 other:days
Unit : mg/kg sediment dw
NOEC : = 90 measured/nominal
LC50 : = 294 measured/nominal
LOEC : = 151 measured/nominal
Method : ASTM E1706-95b sediment toxicity test
Year : 2002
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : Sediment Organism Toxicity, 2% TOC

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and ASTM guidelines.

The objective of this study was to determine the effects of sediment-incorporated TBBPA, in a sediment with total organic carbon content of approximately 2% on the oligochaete, Lumbriculus variegates, during a 28-day exposure period under flow-through conditions. The measured endpoints of the test are survivorship (original organisms and/or offspring) and growth as determined by dry weight measurements.

Groups of oligochaetes were exposed to a geometric series of six test concentrations and a negative control for 28 days under flow-through test conditions. Eight replicate test compartments were maintained in each treatment and control group, with 10 oligochaetes in each test compartment, for a total of 80 oligochaetes per test concentration. Each test compartment contained a quantity of sediment and overlying water. Additional replicates were added in each treatment and control group for analytical sampling of water and sediment. The "analytical" replicates sampled on Day 0 contained no oligochaetes, while oligochaetes were added at test initiation to the "analytical" replicates sampled on Day 7 and at test termination. Nominal test concentrations were 90, 151, 254, 426, 715 and 1200 mg/Kg of sediment based on the dry weight of the sediment. The results of the study are based on the Day 0 nominal test

concentrations. Overlying water, pore water and sediment samples were collected and analyzed from the "analytical replicates" of the control group and the lowest and two highest test concentrations. The collection and analysis were done approximately one hour after the addition of test organisms to the test system on Day 0, on Day 7 and at the end of the test. Results of the analyses were used to confirm the lowest and two highest test concentrations. Test compartments were impartially positioned in a diluter unit approximately 48 hours prior to test initiation to condition the sediment prior to introduction of organisms. Oligochaetes were impartially assigned to exposure compartments at test initiation. Observations of mortality and abnormal behavior were made at least three times per week during the test. Survivorship/reproduction and growth (dry weights) were determined at the end of the 28-day test period. The percent reduction in the numbers of organisms present in the treatment groups at test termination in comparison to the control group was used to determine the 28-day EC50 value. The lowest-observed-effect-concentration (LOEC) and the no-observed-effect-concentration (NOEC) were determined by the concentration-response pattern and statistical analysis of the survival/reproduction and dry weight data.

The 28-day EC50 value for oligochaetes (Lumbriculus variegatus) exposed to TBBPA in sediment was 294 mg/Kg dry weight of sediment. The owest-observed-effect-concentration (LOEC) and the no-observed-effect-concentration (NOEC) were based on evaluation of the survival/reproduction and dry weight data. The most sensitive parameter in this study was survival/reproduction. Based on the results of this study, the LOEC was 151 mg/Kg dry weight of sediment and the NOEC was 90 mg/Kg dry weight of sediment (Krueger et al. 2001).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (44)

09.08.2005

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species : other terrestrial plant: soybean
Endpoint : other: emergence and growth
Exposure period : 21 day(s)
Unit : mg/kg soil dw
NOEC : = 5000 measured/nominal
LOEC : > 5000 measured/nominal
Method : EPA OPPTS 850.4100
Year : 2002
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : Seedling Emergence and Growth in Six Species of Terrestrial Plants

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and OECD guidelines.

The purpose of the study was to determine the effects of TBBPA on the seedling emergence and growth of six species of non-target plants. The experimental design for this study consisted of a negative control and five treatment groups. Each group had four replicate pots with ten seeds

planted in each pot. Test concentrations of TBBPA were made by soil incorporation to each treatment group prior to the planting of seeds. The nominal test substance concentrations were 20, 78, 313, 1250, and 5000 mg of TBBPA per kilogram of dry soil (mg/kg). A control group, which received no test substance incorporation, was maintained concurrently. Seeds were impartially assigned to prelabeled growth pots on the day of test initiation. The replicate pots were placed in a randomized block design on a greenhouse table after planting. Observations of emergence were made on Days 7, 14, and 21. A general assessment of seedling condition was made on Day 7, while observations of height, shoot dry weight, and assignment of plant condition scores were made only on Day 21.

There were no adverse treatment-related effects on soybean seedling growth resulting from soil incorporated TBBPA. Therefore, the NOEC for soybean was the highest concentration tested, 5000 mg/kg, and the LOEC was not determined. Treatment-related effects on seedling growth were observed in corn, cucumber, onion, ryegrass, and tomato. The most sensitive endpoint for corn was seedling dry weight, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. EC25 and EC50 for corn was determined to be >5000 mg/kg. The NOEC and LOEC for both seedling dry weight and height of cucumber - the most sensitive endpoints - were 20 and 78 mg/kg, respectively. The EC25 and EC50 values for dry weight of cucumber were determined to be 73 and 1672 mg/kg, respectively. The most sensitive endpoints for onion were seedling dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The EC25 and EC50 values for onion dry weight were determined to be 460 and 4264 mg/kg, respectively. The most sensitive endpoints for ryegrass were observed in dry weight and height, which resulted in a NOEC of 78 mg/kg, and a LOEC of 313 mg/kg. The EC25 and EC50 values for dry weight were 49 mg/kg and 459 mg/kg, respectively. The most sensitive endpoints for tomato were observed in dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The value for the EC25 for tomato was determined to be 422 mg/kg; the EC50 was determined to be >5000 mg/kg (Porch J et al. 2002).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (45)

Species : other terrestrial plant: corn
Endpoint : other: emergence and growth
Exposure period : 21 day(s)
Unit : mg/kg soil dw
NOEC : = 313 measured/nominal
LOEC : = 1250 measured/nominal
Method : EPA OPPTS 850.4100
Year : 2002
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : Seedling Emergence and Growth in Six Species of Terrestrial Plants

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and OECD guidelines.

The purpose of the study was to determine the effects of TBBPA on the seedling emergence and growth of six species of non-target plants. The experimental design for this study consisted of a negative control and five treatment groups. Each group had four replicate pots with ten seeds planted in each pot. Test concentrations of TBBPA were made by soil

incorporation to each treatment group prior to the planting of seeds. The nominal test substance concentrations were 20, 78, 313, 1250, and 5000 mg of TBBPA per kilogram of dry soil (mg/kg). A control group, which received no test substance incorporation, was maintained concurrently. Seeds were impartially assigned to prelabeled growth pots on the day of test initiation. The replicate pots were placed in a randomized block design on a greenhouse table after planting. Observations of emergence were made on Days 7, 14, and 21. A general assessment of seedling condition was made on Day 7, while observations of height, shoot dry weight, and assignment of plant condition scores were made only on Day 21.

There were no adverse treatment-related effects on soybean seedling growth resulting from soil incorporated TBBPA. Therefore, the NOEC for soybean was the highest concentration tested, 5000 mg/kg, and the LOEC was not determined. Treatment-related effects on seedling growth were observed in corn, cucumber, onion, ryegrass, and tomato. The most sensitive endpoint for corn was seedling dry weight, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. EC25 and EC50 for corn was determined to be >5000 mg/kg. The NOEC and LOEC for both seedling dry weight and height of cucumber - the most sensitive endpoints - were 20 and 78 mg/kg, respectively. The EC25 and EC50 values for dry weight of cucumber were determined to be 73 and 1672 mg/kg, respectively. The most sensitive endpoints for onion were seedling dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The EC25 and EC50 values for onion dry weight were determined to be 460 and 4264 mg/kg, respectively. The most sensitive endpoints for ryegrass were observed in dry weight and height, which resulted in a NOEC of 78 mg/kg, and a LOEC of 313 mg/kg. The EC25 and EC50 values for dry weight were 49 mg/kg and 459 mg/kg, respectively. The most sensitive endpoints for tomato were observed in dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The value for the EC25 for tomato was determined to be 422 mg/kg; the EC50 was determined to be >5000 mg/kg (Porch J et al. 2002).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (45)

Species : other terrestrial plant: cucumber
Endpoint : other: emergence and growth
Exposure period : 21 day(s)
Unit : mg/kg soil dw
NOEC : = 20 measured/nominal
LOED : = 78 measured/nominal
Method : EPA OPPTS 850.4100
Year : 2002
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : Seedling Emergence and Growth in Six Species of Terrestrial Plants

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and OECD guidelines.

The purpose of the study was to determine the effects of TBBPA on the seedling emergence and growth of six species of non-target plants. The experimental design for this study consisted of a negative control and five treatment groups. Each group had four replicate pots with ten seeds planted in each pot. Test concentrations of TBBPA were made by soil incorporation to each treatment group prior to the planting of seeds. The

nominal test substance concentrations were 20, 78, 313, 1250, and 5000 mg of TBBPA per kilogram of dry soil (mg/kg). A control group, which received no test substance incorporation, was maintained concurrently. Seeds were impartially assigned to prelabeled growth pots on the day of test initiation. The replicate pots were placed in a randomized block design on a greenhouse table after planting. Observations of emergence were made on Days 7, 14, and 21. A general assessment of seedling condition was made on Day 7, while observations of height, shoot dry weight, and assignment of plant condition scores were made only on Day 21.

There were no adverse treatment-related effects on soybean seedling growth resulting from soil incorporated TBBPA. Therefore, the NOEC for soybean was the highest concentration tested, 5000 mg/kg, and the LOEC was not determined. Treatment-related effects on seedling growth were observed in corn, cucumber, onion, ryegrass, and tomato. The most sensitive endpoint for corn was seedling dry weight, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. EC25 and EC50 for corn was determined to be >5000 mg/kg. The NOEC and LOEC for both seedling dry weight and height of cucumber - the most sensitive endpoints - were 20 and 78 mg/kg, respectively. The EC25 and EC50 values for dry weight of cucumber were determined to be 73 and 1672 mg/kg, respectively. The most sensitive endpoints for onion were seedling dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The EC25 and EC50 values for onion dry weight were determined to be 460 and 4264 mg/kg, respectively. The most sensitive endpoints for ryegrass were observed in dry weight and height, which resulted in a NOEC of 78 mg/kg, and a LOEC of 313 mg/kg. The EC25 and EC50 values for dry weight were 49 mg/kg and 459 mg/kg, respectively. The most sensitive endpoints for tomato were observed in dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The value for the EC25 for tomato was determined to be 422 mg/kg; the EC50 was determined to be >5000 mg/kg (Porch J et al. 2002).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (45)

Species : other terrestrial plant: onion
Endpoint : other: emergence and growth
Exposure period : 21 day(s)
Unit : mg/kg soil dw
NOEC : = 313 measured/nominal
LOEC : = 1250 measured/nominal
Method : EPA OPPTS 850.4100
Year : 2002
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : Seedling Emergence and Growth in Six Species of Terrestrial Plants

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and OECD guidelines.

The purpose of the study was to determine the effects of TBBPA on the seedling emergence and growth of six species of non-target plants. The experimental design for this study consisted of a negative control and five treatment groups. Each group had four replicate pots with ten seeds planted in each pot. Test concentrations of TBBPA were made by soil incorporation to each treatment group prior to the planting of seeds. The nominal test substance concentrations were 20, 78, 313, 1250, and 5000

mg of TBBPA per kilogram of dry soil (mg/kg). A control group, which received no test substance incorporation, was maintained concurrently. Seeds were impartially assigned to prelabeled growth pots on the day of test initiation. The replicate pots were placed in a randomized block design on a greenhouse table after planting. Observations of emergence were made on Days 7, 14, and 21. A general assessment of seedling condition was made on Day 7, while observations of height, shoot dry weight, and assignment of plant condition scores were made only on Day 21.

There were no adverse treatment-related effects on soybean seedling growth resulting from soil incorporated TBBPA. Therefore, the NOEC for soybean was the highest concentration tested, 5000 mg/kg, and the LOEC was not determined. Treatment-related effects on seedling growth were observed in corn, cucumber, onion, ryegrass, and tomato. The most sensitive endpoint for corn was seedling dry weight, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. EC25 and EC50 for corn was determined to be >5000 mg/kg. The NOEC and LOEC for both seedling dry weight and height of cucumber - the most sensitive endpoints - were 20 and 78 mg/kg, respectively. The EC25 and EC50 values for dry weight of cucumber were determined to be 73 and 1672 mg/kg, respectively. The most sensitive endpoints for onion were seedling dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The EC25 and EC50 values for onion dry weight were determined to be 460 and 4264 mg/kg, respectively. The most sensitive endpoints for ryegrass were observed in dry weight and height, which resulted in a NOEC of 78 mg/kg, and a LOEC of 313 mg/kg. The EC25 and EC50 values for dry weight were 49 mg/kg and 459 mg/kg, respectively. The most sensitive endpoints for tomato were observed in dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The value for the EC25 for tomato was determined to be 422 mg/kg; the EC50 was determined to be >5000 mg/kg (Porch J et al. 2002).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (45)

Species : Lolium perenne (Monocotyledon)
Endpoint : other: emergence and growth
Exposure period : 21 day(s)
Unit : mg/kg soil dw
NOEC : = 78 measured/nominal
LOEC : = 313 measured/nominal
Method : EPA OPPTS 850.4100
Year : 2002
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : Seedling Emergence and Growth in Six Species of Terrestrial Plants

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and OECD guidelines.

The purpose of the study was to determine the effects of TBBPA on the seedling emergence and growth of six species of non-target plants. The experimental design for this study consisted of a negative control and five treatment groups. Each group had four replicate pots with ten seeds planted in each pot. Test concentrations of TBBPA were made by soil incorporation to each treatment group prior to the planting of seeds. The nominal test substance concentrations were 20, 78, 313, 1250, and 5000 mg of TBBPA per kilogram of dry soil (mg/kg). A control group, which

received no test substance incorporation, was maintained concurrently. Seeds were impartially assigned to prelabeled growth pots on the day of test initiation. The replicate pots were placed in a randomized block design on a greenhouse table after planting. Observations of emergence were made on Days 7, 14, and 21. A general assessment of seedling condition was made on Day 7, while observations of height, shoot dry weight, and assignment of plant condition scores were made only on Day 21.

There were no adverse treatment-related effects on soybean seedling growth resulting from soil incorporated TBBPA. Therefore, the NOEC for soybean was the highest concentration tested, 5000 mg/kg, and the LOEC was not determined. Treatment-related effects on seedling growth were observed in corn, cucumber, onion, ryegrass, and tomato. The most sensitive endpoint for corn was seedling dry weight, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. EC25 and EC50 for corn was determined to be >5000 mg/kg. The NOEC and LOEC for both seedling dry weight and height of cucumber - the most sensitive endpoints - were 20 and 78 mg/kg, respectively. The EC25 and EC50 values for dry weight of cucumber were determined to be 73 and 1672 mg/kg, respectively. The most sensitive endpoints for onion were seedling dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The EC25 and EC50 values for onion dry weight were determined to be 460 and 4264 mg/kg, respectively. The most sensitive endpoints for ryegrass were observed in dry weight and height, which resulted in a NOEC of 78 mg/kg, and a LOEC of 313 mg/kg. The EC25 and EC50 values for dry weight were 49 mg/kg and 459 mg/kg, respectively. The most sensitive endpoints for tomato were observed in dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The value for the EC25 for tomato was determined to be 422 mg/kg; the EC50 was determined to be >5000 mg/kg (Porch J et al. 2002).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (45)

Species : other terrestrial plant: tomato
Endpoint : other: emergence and growth
Exposure period : 21 day(s)
Unit : mg/kg soil dw
NOEC : = 313 measured/nominal
LOEC : = 1250 measured/nominal
Method : EPA OPPTS 850.4100
Year : 2002
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : Seedling Emergence and Growth in Six Species of Terrestrial Plants

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and OECD guidelines.

The purpose of the study was to determine the effects of TBBPA on the seedling emergence and growth of six species of non-target plants. The experimental design for this study consisted of a negative control and five treatment groups. Each group had four replicate pots with ten seeds planted in each pot. Test concentrations of TBBPA were made by soil incorporation to each treatment group prior to the planting of seeds. The nominal test substance concentrations were 20, 78, 313, 1250, and 5000 mg of TBBPA per kilogram of dry soil (mg/kg). A control group, which received no test substance incorporation, was maintained concurrently.

Seeds were impartially assigned to prelabeled growth pots on the day of test initiation. The replicate pots were placed in a randomized block design on a greenhouse table after planting. Observations of emergence were made on Days 7, 14, and 21. A general assessment of seedling condition was made on Day 7, while observations of height, shoot dry weight, and assignment of plant condition scores were made only on Day 21.

There were no adverse treatment-related effects on soybean seedling growth resulting from soil incorporated TBBPA. Therefore, the NOEC for soybean was the highest concentration tested, 5000 mg/kg, and the LOEC was not determined. Treatment-related effects on seedling growth were observed in corn, cucumber, onion, ryegrass, and tomato. The most sensitive endpoint for corn was seedling dry weight, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. EC25 and EC50 for corn was determined to be >5000 mg/kg. The NOEC and LOEC for both seedling dry weight and height of cucumber - the most sensitive endpoints - were 20 and 78 mg/kg, respectively. The EC25 and EC50 values for dry weight of cucumber were determined to be 73 and 1672 mg/kg, respectively. The most sensitive endpoints for onion were seedling dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The EC25 and EC50 values for onion dry weight were determined to be 460 and 4264 mg/kg, respectively. The most sensitive endpoints for ryegrass were observed in dry weight and height, which resulted in a NOEC of 78 mg/kg, and a LOEC of 313 mg/kg. The EC25 and EC50 values for dry weight were 49 mg/kg and 459 mg/kg, respectively. The most sensitive endpoints for tomato were observed in dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The value for the EC25 for tomato was determined to be 422 mg/kg; the EC50 was determined to be >5000 mg/kg (Porch J et al. 2002).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (45)

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

Type	:	artificial soil
Species	:	Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint	:	other: survival
Exposure period	:	28 day(s)
Unit	:	mg/kg soil dw
NOEC	:	= 4840 measured/nominal
LC50	:	> 4840 measured/nominal
Method	:	
Year	:	2003
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : Earthworm Survival (28 days) and Reproduction (56 days)

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and OECD guidelines.

The potential effects of TBBPA on the survival and reproduction of the earthworm, Eisenia fetida, was investigated in a 56-day study in artificial soil. The artificial soil was characterized as a sandy loam (79% sand, 10% silt, 12% clay) with an organic matter (carbon) content of 7.7 (4.5). For determining effects on survival (28 day exposure), the nominal test

concentrations were 0 (Control), 313, 625, 1,250, 2,500, and 5,000 mg TBBPA/kg dry soil, and the corresponding measured concentrations (HPLC/UV) were <100, 362, 640, 1,250, 2,430, and 4,840 mg TBBPA/kg dry soil. For determining reproductive effects (56 day exposure), the nominal test concentrations were 0 (Control), 0.63, 1.3, 2.5, 5.0, 10, 20, and 40 mg TBBPA/kg dry soil and the corresponding mean measured test concentrations (HPLC/MS) were <0.100, 0.562, 1.16, 2.11, 4.50, 9.01, 16.7, and 35.4 mg TBBPA/kg dry soil.

In the reproductive portion of the study, mean measured tissue concentrations in the worms (HPLC/MS) collected on Day 28 were <0.250 (control), 2.86, 0.279, 0.394, 0.456, 0.453, 0.611, and 0.677 mg TBBPA per gram of tissue, respectively. This corresponds to bioaccumulation factors (concentration in tissues divided by soil concentration) of 5, 0.2, 0.2, 0.1, 0.05, 0.04 and 0.02, respectively.

The NOECsurvival was 4,840 mg/kg dry soil. The 28-Day EC10 and E50survival was > 4,840 mg/kg dry soil. The NOECreproduction was 2.11 mg/kg dry soil with a 56-Day EC10reproduction of 0.14 mg/kg dry soil and a 56-Day EC50reproduction of 1.9 mg/kg dry soil. Although the bioaccumulation factor of the low treatment level was greater than 1.0, the decrease in bioaccumulation factors with increasing soil concentration suggests that TBBPA did not bioaccumulate within the worm tissues during the 28-day exposure (Aufterhiede J et al. 2003).

Reliability : (1) valid without restriction
09.08.2005 (46)

Type : artificial soil
Species : Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint : other: reproduction
Exposure period : 56 day(s)
Unit : mg/kg soil dw
NOEC : = 2.11 measured/nominal
LC50 : = 1.9 measured/nominal
Method :
Year : 2003
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : Earthworm Survival (28 days) and Reproduction (56 days)

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and OECD guidelines.

The potential effects of TBBPA on the survival and reproduction of the earthworm, Eisenia fetida, was investigated in a 56-day study in artificial soil. The artificial soil was characterized as a sandy loam (79% sand, 10% silt, 12% clay) with an organic matter (carbon) content of 7.7 (4.5). For determining effects on survival (28 day exposure), the nominal test concentrations were 0 (Control), 313, 625, 1,250, 2,500, and 5,000 mg TBBPA/kg dry soil, and the corresponding measured concentrations (HPLC/UV) were <100, 362, 640, 1,250, 2,430, and 4,840 mg TBBPA/kg dry soil. For determining reproductive effects (56 day exposure), the nominal test concentrations were 0 (Control), 0.63, 1.3, 2.5, 5.0, 10, 20, and 40 mg TBBPA/kg dry soil and the corresponding mean measured test concentrations (HPLC/MS) were <0.100, 0.562, 1.16, 2.11, 4.50, 9.01, 16.7, and 35.4 mg TBBPA/kg dry soil.

In the reproductive portion of the study, mean measured tissue

concentrations in the worms (HPLC/MS) collected on Day 28 were <0.250 (control), 2.86, 0.279, 0.394, 0.456, 0.453, 0.611, and 0.677 mg TBBPA per gram of tissue, respectively. This corresponds to bioaccumulation factors (concentration in tissues divided by soil concentration) of 5, 0.2, 0.2, 0.1, 0.05, 0.04 and 0.02, respectively.

The NOECsurvival was 4,840 mg/kg dry soil. The 28-Day EC10 and E50survival was > 4,840 mg/kg dry soil. The NOECreproduction was 2.11 mg/kg dry soil with a 56-Day EC10reproduction of 0.14 mg/kg dry soil and a 56-Day EC50reproduction of 1.9 mg/kg dry soil. Although the bioaccumulation factor of the low treatment level was greater than 1.0, the decrease in bioaccumulation factors with increasing soil concentration suggests that TBBPA did not bioaccumulate within the worm tissues during the 28-day exposure (Aufterhiede J et al. 2003).

09.08.2005 (46)

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

Species	:	Coturnix coturnix japonica (avian)
Endpoint	:	other: reproductive behavior, distribution
Exposure period	:	
Unit	:	
Method	:	other
Year	:	2001
GLP	:	no data
Test substance	:	other TS:14C-TBBPA
Attached document	:	Reproduction and Distribution in Japanese Quail

The potential for TBBPA to affect reproduction variables in adult Japanese quails following in ovo exposure as well as TBBPA's distribution in eggs, embryos and laying birds was investigated using 14C-labelled material. Uptake of 14C-TBBPA was studied in 6- and 9-day-old quail embryos, by beta-spectrometry, following egg-injection (1.9 ug/g egg) on day 3. TBBPA's distribution in quail embryos (1.9 ug/g egg) and adult females (oral and intravenous, 250 ug/bird) was studied using tape-section autoradiography following a single dose. The potential for effects on male sexual behavior, testis weight, plasma testosterone concentration, egg-laying, and gross morphology of the oviducts was evaluated in adult birds following embryonic exposure (15 ug/g egg).

The embryonic uptake of TBBPA was low (< 1% of the radiolabel) after yolk injection on day 3 of incubation. Its distribution pattern was characterized by a strong retention in the yolk at all time points, although evidence for metabolism was detected (labeling in the liver, bile and allantoic fluid). Thus, TBBPA's transfer to the embryo from the yolk was low, and any transferred TBBPA was rapidly metabolized and readily excreted.

In laying quail, orally or intravenously administered TBBPA was rapidly eliminated via bile and excreted in feces, and transfer to egg yolks was low. Thus, TBBPA was readily excreted by the laying female as well as by the growing embryo, and consequently, the risk for embryonic exposure following dietary intake in laying birds is expected to be low.

In ovo exposure to TBBPA (15 ug/g egg) did not cause estrogen-like effects in the adult quail. Egg-laying was not affected in female birds, and no effect in male quail on sexual behavior, testis weight or plasma testosterone was detected. (Halldin K et al. 2001.)

Another study by the same group also reported that TBBPA (45 ug/g quail egg) did not induce estrogenic-like effects (Berg et al. 2001)

Flag : Risk Assessment
10.08.2005 (47) (48)

Species : Coturnix coturnix japonica (avian)
Endpoint : other: estrogen-like effects on sex organ development
Exposure period :
Unit : other:ug/egg
NOEC : >= 45 measured/nominal
Method : other
Year : 2001
GLP : no data
Test substance : no data

Attached document : Estrongenic-like Effects in Japanese Quail

TBBPA (45 ug/g quail egg) did not induce estrogenic-like effects (Berg et al. 1999).

TBBPA was injected into the egg yolk of quail and chicken eggs early during incubation and the embryos examined 2 days before anticipated hatching. No estrogen-like effects were observed. A high embryo morality occured in both species.

Flag : Risk Assessment
10.08.2005 (49)

Species : Coturnix coturnix japonica (avian)
Endpoint : other
Exposure period :
Unit : other:ug/egg
NOEC : > 15 measured/nominal
Method : other
Year : 2005
GLP : no data
Test substance : no data

Attached document : Sexual Differntiation and Reproductive Function in Japanese Quail

TBBPA (15 ug/egg) had no effect on sexual behavior or reproductive organ morphology in adult male Japanese quail exposed via egg yolk injection on day 3 of incubation. Sexual behaviors tested at age 9 weeks for 5 consecutive days included: neck grab, mount attempt, mount, cloacal contact movement. Additional parameters evaulated included cloacal gland area measurement, plasma testosterone, testis weights, gonado-somatic index, testicular histopathology. TBBPA did not cause any significant estrogen-like effects on sexual behavior, gonado-somatic index, testis weight asymmetry, or plasma testosterone. Body weight was not affected (Halldin et al 2005).

Flag : Risk Assessment
10.08.2005 (50)

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

Type : other
Deg. product :

Attached document : Several studies have investigated TBBPA's potential for absorption and elimination in environmentally relevant species.

Data in earthworms suggests TBBPA did not bioaccumulate following exposure via the soil (Section 4.6.3).

After oral exposure of quail, TBBPA was rapidly eliminated via bile and excreted in feces, and transfer to egg yolks was low (Section 4.6.4). After egg yolk injection, TBBPA's transfer to the growing embryo was low, and that amount transferred was readily excreted by the embryo. Thus, the risk for bioaccumulation or embryonic exposure following dietary intake in laying birds is expected to be low.

After exposure to TBBPA in water, fish rapidly reached steady-state tissue concentrations with measured BCFs of < 500 (Section 3.7). Fish also rapidly eliminated TBBPA once removed to fresh water.

Based on these studies, TBBPA appears to have little potential to bioconcentrate or bioaccumulate in earthworm, birds or fish. This is likely related to the organisms' ability to metabolize TBBPA to readily eliminated forms.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005

4.9 ADDITIONAL REMARKS

Memo : Amphibian (Frog) Thyroid Hormone System

Attached document : The potential for TBBPA to adversely affect the amphibian thyroid hormone system was investigated using the tadpole (Xenopus) tail regression assay. Tadpoles were microinjected with TBBPA at developmental stage 58 (hind limbs emerged; forelimbs formed, but not emerged) at doses up to 60 ug/tadpole.

Tail resorption was not affected by TBBPA. Positive controls showed delayed tail resorption (Balch and Metcalfe 2001).

09.08.2005 (51)

Memo : Frog Embryo Teratogenic Assay

Attached document : The potential effect of TBBPA in the frog embryo teratogenisis assay: Xenopus (FETAX) bioassay was assessed. The FETAX bioassay is used for study of potentially hormonally active agents and examines the effects of aqueous agents on the Xenopus embryo during the first 96 hours of development. The endpoints examined include mortality, malformation rate, and growth inhibition/acceleration as indicated by a change in embryo length and the presence of features indicative of earlier/later stages.

Under 2 different growth conditions, standard and minimal levels of sodium and potassium required to prevent developmental retardation, 0.1, 1, 10 100 or 500 ppb TBBPA had no effect on Xenopus development (Garber et al. 2001).

09.08.2005 (52)

Memo : In vitro Binding and Frog Metamorphisis

Attached document : The potential for TBBPA in vitro to a) interact with the thyroid hormone receptor, and b) exhibit thyroid hormonal activity was investigated. In

addition, TBBPA's potential to effect metamorphosis in the frog was investigated.

The IC50 for T3 in the in vitro thyroid hormone receptor assay was 3.28 x 10-9 M; the IC50 for TBBPA in comparison was 3.5 x 10-3 M. Thus, TBBPA was approximately 1 million times less potent than T3 in interacting with the thyroid hormone receptor.

TBBPA had no agonistic effect in vitro on T3 activity in the luciferase reporter assay in CHO-K1 cells. Antagonistic activity was reported at concentrations >= 6.3 uM or >25 uM in the TRalpha1 and TRbeta1 transfected CHO-K1 cells.

When added to water at concentrations ranging from 10-6 to 10-8 M, TBBPA had no effect on the rate of tail shortening in tadpoles (Rana rugosa). T3, added to water at 5 x 10-8 M, induced tail shortening (length reduced by 40% by day 4). TBBPA, at 10-6-10-8M in water, in the presence T3 water concentrations of 5 x 10-8 M, reduced the rate of tail shortening in tadpoles (Kitamura et al. 2005).

11.08.2005 (53)

Memo : Juvenile Rainbow Trout Hepatic Enzymes

Attached document : The potential for TBBPA to effect selected hepatic detoxification and antioxidant enzymes, the liver somatic index, levels of the yolk precursor vitellogen in blood plasma and DNA-adducts was investigated in juvenile rainbow trout. This study is only briefly reported and the experimental details and results are not clearly described.

The fish were injected with TBBPA in peanut oil (0.1, 1, 10, 50, 100, 500 mg/kg in peanut oil), and end points investigated at 1, 4, 14 and 28 days. The paper stated that the highest dose was chosen as one magnitude lower than the oral LD50 for rats and mice "which was around 5 g/kg". In the 28 day experiment, one group was also injected on day 14 with 100 mg/kg, while another group received only one injection of pure peanut oil on day 14. The endpoints included liver somatic index (LSI; liver to body weight ratio), CYP1A, glutathione S transferase (GST), uridine diphosphate glucuronosyl transferase (UDPGT), glutathione reductase (GR), catalase, glutathione peroxidase, blood vitellogenin. The potential for TBBPA to inhibit EROD activity in vitro was also investigated. Wild-caught eelpout were also treated with 100 mg/kg.

TBBPA reportedly induced hepatic GR activity a dose of 100 mg/kg. A trend toward inhibition of CYP1A's EROD activity was reported. Vitellogen levels were not altered which is indicative of a lack of estrogenic effect. The authors considered the lack of toxicity in trout in this study, compared to other studies where exposure to TBBPA occured via water, to be due the route of administration (IP) which presented the test article to the liver prior to distribution to the rest of the organism.

No effect on any endpoint studied in eelpout was observed (Ronisz et al. 2001).

12.08.2005 (54)

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In Vitro/in vivo : In vivo
Type : Toxicokinetics
Species : rat
Number of animals
Males : 10
Females : 0
Doses
Males : 2 mg/kg bw; 1 uCi/rat
Females :
Vehicle : peanut oil
Route of administration : gavage
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:
2nd:
3rd:
Toxic behaviour :
Deg. product :
Method : other
Year : 2000
GLP : no
Test substance : other TS: 14C-TBBPA

Attached document : Rat Absorption, Metabolism, Elimination Study (14C-TBBPA)

In the rat, TBBPA was readily absorbed, metabolized and eliminated within 72 hours after oral dosing. Recovery of 14C-activity in the conventional (n=10) and bile-cannulated (n=8) rat administered a single oral dose of 14C-TBBPA was 92 and 98.5% of the dose, respectively, by 72 hours post-dosing. Owing to the extensive elimination, total tissue retention at 72 hours was limited. In the conventional rat, 2% of the dose was retained in the tissues, but <1% in the cannulated rat at 72 hours. Essentially no deposition of TBBPA was detected in adipose tissue, heart, spleen, testis or thymus (<0.0005% of dose).

The primary route of elimination was the feces; only negligible amounts were detected in urine. Glucuronic acid and sulphate ester conjugates were detected in bile; however, the parent molecule was the predominant form found in feces due to deconjugation by intestinal bacteria (Haak et al. 2000; Larsen et al 1990).

Earlier work concluded that in rats, after oral dosing, approximately 95 percent of the administered material was found in the feces and less than 1.1 percent in the urine within 72 hours. Blood and tissue levels were extremely low at all time points measured. The half-life in the blood was about 20 hours; the maximum half life in any tissue was less than 3 days. Because of the short half-life, the small amounts of TBBPA absorbed would have relatively little persistence or accumulation in mammalian systems (WHO 1995).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
11.08.2005 (55) (56) (57)

In Vitro/in vivo : In vivo
Type : Toxicokinetics

Species : human
Number of animals
Males : 3
Females : 2
Doses
Males : 0.1 mg/kg bw
Females : 0.1 mg/kg bw
Vehicle :
Route of administration : other: gel capsule
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st.:
2nd.:
3rd.:
Toxic behaviour :
Deg. product :
Method : other
Year : 2005
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Attached document : Human Metabolism and Clearance

In humans, TBBPA is rapidly metabolized. A single oral dose of 0.1 mg/kg was administered in a gel capsule to 3 male and 2 female volunteers. Urine and blood concentrations of TBBPA and its metabolites were determined by LC/MS-MS.

The parent TBBPA molecule was not detected in plasma at any time point. The glucuronide and sulfate conjugates of TBBPA were detected in blood and urine. TBBPA-glucuronide was detected in all volunteers, whereas TBBPA-sulfate was detected in only 2 of the 5. Maximum plasma concentrations of the TBBPA-glucuronide (10-15 pmol/ml) were found 2 hrs post-dosing. The glucuronide conjugate was cleared from the blood with an apparent half-life of 26 hrs. In the 2 individuals where the sulfate conjugate was detected, Maximum concentration of the sulfate conjugate in the 2 individuals were detected 4 hr post dosing and declined to the limit of detection after 8 hrs. Only TBBPA-glucuronide was detected in the urine. Approx. 25% of the administered dose was eliminated in the urine. Most of the TBBPA-glucuronide was thought to be eliminated in the feces (Dekant et al. 2005)

Reliability : (1) valid without restriction
Flag : Risk Assessment
11.08.2005 (58)

In Vitro/in vivo : In vitro
Type : Absorption
Species : human
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle : other: acetone
Route of administration : dermal
Exposure time : 8 hour(s)
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :

Half-lives	:	1st: 2nd: 3rd:
Toxic behaviour	:	
Deg. product	:	
Method	:	other: OECD 428
Year	:	2005
GLP	:	yes
Test substance	:	other TS: 14C-TBBPA

Attached document : In vitro Percutaneous Absorption

This study was sponsored by the ACC Brominated Flame Retardant Industry Panel (BFRIP).

An in vitro study was conducted using 14C-TBBPA to assess the rate and extent of absorption following topical application to human skin.

An initial investigation using ethanol as the delivery vehicle and washing the skin with dilute soap was found to provide results unrepresentative of a realistic expsoure scenario. In a repeat study, TBBPA was applied to the skin in an acetone vehicle, and washed from the skin at the end of the 8 hour exposure period.

In the study, split-thickness skin memberanes were mounted into flow-through diffusion cells. Receptor fluid (physiological saline) was pumped underneath the skin at ta flow rate of ca. 1.5 ml/h, and a tritiated water barrier integrity test performed. The skin surface temperature was maintained at ca 32 degrees C throughtout. All skin sampels with a trititated water permeability coefficient < 2.5 x 10-3 cm/h were accepted into the study. The receptor fluid was then changed to ethanol:water (1:1, v/v).

14C-TBBPA (1.9 mg/cm2) was applied in vitro in an acetone vehicle at 10 uL/c2 to the human split-thickness skin membranes mounted in the flow-thr9ugh diffusion cells. The acetone rapidly evaporated.

Absorption was assessed by collecting receptor fluid in hourly fractions from 0-8 h post dose and then in 2 hourly fractions from 8-24 h post dose. At 8 h post dose, the exposure was terminated by washing the skin with liquid soap and rinsed with water. At 24 h post dose, the cells were dismantled and the stratum corneum removed using 25 successive tape strips. All samples were analyzed by liquid scintillation counting.

The absorbed dose and dermal delivery were 0.73% (14.6 ug equiv./cm2) and 1.6% (32.05 ug equiv./cm2) of the applied dose, respectively. At 8 h post dose, the dislodgeable dose was 61.52% of the applied dose. At 24 h post dose, a further 28.01% was dislodged from the skin. Thus, the total dislodgeable dose was 89.53% of the applied dose. The stratum corneum contained a further 12.48% of the applied dose. The bulk of this (9.47%) was recovered in the first 5 tape strips. Since the bulk of the stratum corneum-associated material was found in the first 5 tape strips, 14C-TBBPA was on the surface of the skin and the stratum corneum was an efficient barrier to its penetration (Roper 2005).

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (59)

In Vitro/in vivo	:	In vivo
Type	:	Toxicokinetics
Species	:	rat
Number of animals		

Males	:	
Females	:	
Doses		
Males	:	
Females	:	
Vehicle	:	other:olive oil
Route of administration	:	i.p.
Exposure time	:	
Product type guidance	:	
Decision on results on acute tox. tests	:	
Adverse effects on prolonged exposure	:	
Half-lives	:	1st.: 2nd.: 3rd.:
Toxic behaviour	:	
Deg. product	:	
Method	:	other
Year	:	2001
GLP	:	no data
Test substance	:	other TS: 14C-TBBPA

Attached document : Disposition and Metabolism After a Single IP Dose

Dose = 250 or 1000 mg/kg bw in olive oil

Rat strain/gender not specified.
n=4 rats.

According to the authors, TBBPA administered IP in high, single doses was readily absorbed into the blood, distributed in body organs and elminated. During 72 h following administration, 51-65% of the given 14C-dose was excreted in feces, only a slight anmount (0.3%) in the urine. The 14C-activity in feces was identified as TBBPA (~90%) and tribromobisphenol A (~10%). The identity of 14C-activity in blood or organs was not determined. The authors concluded their results were similar to those reported by Brady as cited in the WHO 1995 report.

Reliability : (2) valid with restrictions

11.08.2005 (60)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	> 5000 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	CMC
Doses	:	5000 mg/kg bw
Method	:	other: limit test
Year	:	1981
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : The oral LD50 in the rat (5M/5F) is >5,000 mg/kg and the dermal LD50 in rabbits is > 2,000 mg/kg. TBBPA is not irritating to the skin or eye. These acute studies were reported in WHO 1995.

Reliability : (1) valid without restriction

Flag : Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (61) (14)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	> 2000 mg/kg bw
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male/female
Number of animals	:	10
Vehicle	:	physiol. saline
Doses	:	2000 mg/kg bw
Method	:	other: limit test
Year	:	1981
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	The oral LD50 in the rat is >5,000 mg/kg and the dermal LD50 in rabbits is > 2,000 mg/kg. TBBPA is not irritating to the skin or eye. These acute studies were reported in WHO 1995.
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (62) (14)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	500 mg
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	0
Result	:	not irritating
Classification	:	not irritating
Method	:	Draize Test
Year	:	1981
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	The oral LD50 in the rat is >5,000 mg/kg and the dermal LD50 in rabbits is > 2,000 mg/kg. TBBPA is not irritating to the skin or eye. These acute studies were reported in WHO 1995.
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (63) (14)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted

Dose	:	100 other:mg
Exposure time	:	
Comment	:	other: not rinsed; examined at 1, 24, 48 and 72 hrs and 7 d after treatment
Number of animals	:	6
Vehicle	:	none
Result	:	not irritating
Classification	:	not irritating
Method	:	Draize Test
Year	:	1981
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	The oral LD50 in the rat is >5,000 mg/kg and the dermal LD50 in rabbits is > 2,000 mg/kg. TBBPA is not irritating to the skin or eye. These acute studies were reported in WHO 1995.
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (64) (14)

5.3 SENSITIZATION

Type	:	other
Species	:	guinea pig
Number of animals	:	10
Vehicle	:	
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	other
Year	:	1981
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Attached document	:	Delayed Contact Hpersensitivity in Guinea Pigs TBBPA (500 mg/induction site) was dermally applied to 10 guinea pigs for a total of nine 6 hr insult periods. A positive contol group (n-10) was treated with 2,4-dinitrochlorobenzene. Appr 14 days after the last sensitizing exposure. The animals were challenged in the smae manner at both the site of sensitizing and a second site. 48-Hr after the first challenge, a second challenge was make.
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (65) (14)

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	90 d
Frequency of treatm.	:	once daily
Post exposure period	:	6 wk
Doses	:	100, 300, 1,000 mg/kg bw
Control group	:	yes, concurrent vehicle
NOAEL	:	= 1000 mg/kg bw
Method	:	EPA OTS 798.2650

Year : 2001
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : Rat 90-Day Subchronic Oral (Gavage)

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and OECD guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel.

This study was conducted to evaluate the subchronic toxicity of TBBPA in CD® [Crl: CD® (SD) IGS BR] rats. The study consisted of three treatment groups and one vehicle (corn oil) control group (ten rats/sex/group). Recovery animals (five rats/sex) were included in the control and high-dose group and evaluated over a 6-week post-treatment period. TBBPA was administered orally by gavage daily for 13 weeks at dose levels of 0, 100,300, and 1000 mg/kg/day at a constant volume of 5 mL/kg/day. The control animals received the vehicle at the same volume and dosing regimen as the treated groups. Animals were observed daily cage side for survivability, injury, and availability of feed and water. Other observations conducted weekly during the study included detailed physical and neurobehavioral evaluations, and measurements of body weights and food consumption. A Functional Observational Battery (FOB) was conducted pretest and at Week 12. Motor activity (MA) was also evaluated during Week 12. Ophthalmoscopic examinations were conducted pretest, study termination, and following recovery .Other evaluations conducted at termination and following recovery included: hematology, clinical chemistry , urinalysis, organ weights, and pathological examinations (macroscopic and microscopic). Thyroid hormone levels [Thyroid Stimulating Hormone (TSH), T3 (3,5,3' -triiodothyronine), and T4 (thyroxine or 3,5,3'5'-tetraiodothyronine)] were evaluated of animals at 33 days and at termination. These same hormone levels were evaluated following recovery.

Homogeneity of the dosing suspensions at the low and high concentration levels was determined on mixes used the first week of study. Mean concentration recoveries from the periodic analyses of dosing suspensions used on study were 102.5%, 110.2%, and 106.8% of nominal for the l00, 300, and 1000 mg/kg/day groups, respectively.

A total of six females (two control and four in the 1000 mg/kg/day group) died or were euthanized in extremis. The mortality/moribundity seen in these groups was considered related to dosing injury and not treatment related.

No effect of treatment was seen in clinical or neurobehavioral evaluations, body weights, food consumption, ophthalmological examinations, MA, FOB evaluations, hematology or urinalysis evaluations. Likewise, no effect of treatment was evident from organ weights, or from the macroscopic or microscopic examinations.

After 90 days of dosing, total bilirubin values were statistically higher than the control means (males: 0.14 ± 0.05; females: 0.13 ± 0.05) in males in the 1000 mg/kg/day dose (0.34 ± 0.024) ($p<0.01$) group and in females in the 300 (0.19 ± 0.03) ($p<0.05$) and 1000 mg/kg/day (0.2 ± 0.06) groups ($p<0.01$). Mean serum alkaline phosphatase (ALP) levels after 90 days of dosing in the female 1000 mg/kg/day (98.9 ± 49.47) group was statistically higher than that of the control mean (58.4 ± 28.46) ($p<0.05$). A slight increase, but non-statistically different, was also observed in males. Although these differences were considered possibly due to test article

administration, neither of these changes was of sufficient magnitude as to be biologically or toxicologically meaningful or adverse. Serum bilirubin and ALP levels in control and treated groups of both sexes were comparable after the end of the recovery period.

With respect to serum hormone levels, mean TSH and T3 levels were statistically comparable between control and treated animals at all time points (Day 33, terminal and recovery euthanasia). Mean T4 levels were statistically lower than the control mean (Day 33: 4.96 ± 0.84; terminal: 5.09 ± 0.80) in the 100 (Day 33: 3.66 ± 0.88; terminal: 3.27 ± 0.67), 300 (Day 33: 3.42 ± 0.71; terminal: 2.61 ± 0.87) and 1000 (Day 33: 3.39 ± 0.55; terminal: 3.09 ± 0.91) mg/kg/day male dose groups at days 33 and 90 ($p<0.01$). Mean T4 1evels were also statistically lower than the control mean (4.27 ± 0.96) in females in the l00 (3.31 ± 1.08), 300 (3.24 ± 0.85) and 1000 (3.33 ± 0.84) mg/kg/day dose groups at Day 33 ($p<0.05$). Mean T4 1evels in all female dose groups were statistically comparable to the control mean at Day 90. At the recovery euthanasia, mean T4 1evels were comparable in the control and 1000 mg/kg/day male and female groups. The change in T41evels seen in the 1000 mg/kg/day group was reversible and levels comparable to control were seen following recovery.

The decrease in serum T 4 levels was considered a possible effect of test article administration. TBBPA has been shown to competitively displace T4 from transthyretin (TTR), a major serum T4-binding protein in the rat, in vitro (Meerts et al. 2000. Toxicological Sciences, 56,95-104). That portion of serum T4 displaced from its binding site would be available for metabolism and elimination, thereby leading to a decrease in serum levels. The half-life of T4 in the rat is short due to its transport by TTR, and thus this species is sensitive to perturbations in T4 levels. For example, the plasma T4 half-life in rats is 12-24 hours while T4's half-life in humans is 5-9 days (Capen, C. 1996. Chapter 21. Toxic Responses of the Endocrine System. In: Casarett & Doull's Toxicology, The Basic Science of Poisons. Fifth Edition. Ed. Curtis Klaassen. McGraw-Hill, New York. 474-006). In humans circulating T4 is bound primarily to thyroxin binding globulin, but this high affinity binding protein is not present in rodents. This mechanism, displacement of T4 from TTR-binding by TBBPA with subsequent metabolism and elimination in the liver, may account for the decreased mean serum T4 levels in treated animals. Because the decrease in T4 1evels was not of sufficient magnitude to alter mean serum TSH or T3 levels, thyroid histopathology, thyroid weight, or other parameters indicative of thyroid pathology (e.g. body weight, etc.), the decrease in serum T4 1evels was not considered adverse. The reduction in serum T4 1evels was not accompanied by evidence of toxicity or adverse effects, and the animals were clinically normal.

Thus, in this rat 90-day oral toxicity study with TBBP A, the No Observed Adverse Effect Level (NOAEL) was 1000 mg/kg/day, the highest dose tested. No effect on mortality, clinical signs, body or organ weights, histopathology, urinalysis, ophthalmology, FOB, MA, serum TSH, serum T3 or serum chemistries was observed. Differences were observed for bilirubin and ALP, but neither of these changes were found to be biologically or toxicologically meaningful or adverse. Serum T4 levels were decreased in treated animals, but the decrease was not of sufficient magnitude to induce adverse effects.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
10.08.2005 (66)

Type : Sub-chronic
Species : rat
Sex : male/female
Strain : Sprague-Dawley

Route of admin.	:	oral feed
Exposure period	:	90 days
Frequency of treatm.	:	continually in the diet
Post exposure period	:	none
Doses	:	0.3, 3, 30, 100 mg/kg bw/d
Control group	:	yes, concurrent no treatment
NOAEL	:	> 100 mg/kg bw
NOEL	:	= 100 ml/kg bw
Method	:	other
Year	:	1975
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : Rat 90 Day Subchronic Oral (Diet)

TBBPA was administered to male and female rats in their diet for 90 days to investigate the possible effects associated with repeated ingestion of the test article. The concentrations of TBBPA in the diet were adjusted so that rats were administered 0, 0.3, 3, 30 or 100 mg/kg/d. The parameters evaluated in all animals included: appearance, demeanor, body weights, and food consumption. In 5 rats/sex/dose, the following were evaluated: routine hematology measurements, clinical chemistry determinations (serum urea nitrogen, alkaline phosphatase activity, serum glutamic pyruvic transminase activity), routine urinalyses, organ weights, organ-to-body weight ratios, and gross and microscopic examination of tissues. On days 10, 20, 30 and 60, 2 rats/sex from the control group and 3 mg/kg/d dose level were sacrificed for bromine content via neutron activation analysis. At study termination (day 90), tissue specimens of liver, kidney, skeletal muscle, fat an dserum were collected and frozen from 2 rats/sex/group for bromine analysis. Two rats/sex/dose continued on study untreated and sacrificed on day 100, 111 or 132 for tissue determination of bromine levels.

No toxicologically significant effects were found. Thus, the administration of TBBPA in the diet of rats at doses up to 100 mg/kg/d for 90 days was not associated with toxicological effects. Evaluation of tissues for bromine from rats receiving 3 mg TBBPA/kg/d for 90 days did not reveal any difference in the bromine content from that in tissues of control rats (Quast and Humiston 1975).

Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (67) (14)

Type	:	Sub-chronic
Species	:	rat
Sex	:	
Strain	:	
Route of admin.	:	oral feed
Exposure period	:	28 days
Frequency of treatm.	:	continually in the feed
Post exposure period	:	2, 6 or 12 weeks
Doses	:	1, 10, 100 or 1000 ppm
Control group	:	yes, concurrent no treatment
NOEL	:	>= 1000 ppm
Method	:	other
Year	:	1972
GLP	:	no
Test substance	:	

Attached document : Rat 28-Day Subcronic Oral (Diet)

In a 28-day oral study, no toxicity was observed in rats treated with up to

1,000 ppm TBBPA in the diet. Rats were fed at dietary dose levels of 0, 1, 10, 100 or 1000 ppm TBBPA for 28 days after which one group was sacrificed and the remaining rats placed on untreated diets for 2, 6 or 12 weeks. No effects on general appearance, behavior, body weight, food consumption or mortality were observed. No compound related gross or microscopic lesions or variations in organ weights were observed at any dose level. Liver and adipose bromine levels were similar in rats of the control and high dose groups sacrificed at the end of the 28 day treatment period. (Goldenthal and Geil 1972; WHO 1995)

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (68) (14)

Type : Sub-chronic
Species : rabbit
Sex :
Strain :
Route of admin. : dermal
Exposure period : 21-days
Frequency of treatm. : 6 hours/day, 5 days/week for 3 weeks
Post exposure period : no
Doses : 100, 500, or 2,500 mg TBBPA/kg body weight
Control group : yes, concurrent no treatment
NOEL : >= 1000 mg/kg bw
Method : other
Year : 1979
GLP : no
Test substance :

Attached document : Rabbit 21-Day Dermal

In a 21-day dermal study, no systemic toxicity was observed in rabbits treated with 0, 100, 500, or 2,500 mg TBBPA/kg body weight for 6 hours/day, 5 days/week for 3 weeks. No mortality or overt signs of toxicity were observed. Body weight gain, hematological parameters, urinalysis, organ weights, and gross and microscopic examinations did not reveal any compound-related changes. (Goldenthal et al. 1979; WHO 1995)

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (69) (14)

Type : Sub-chronic
Species : rat
Sex :
Strain :
Route of admin. : inhalation
Exposure period : 14 days
Frequency of treatm. : 4 h daily, 5 days/week for 2 weeks
Post exposure period : no
Doses : 2000, 6000, or 18,000 mg/m3
Control group : yes, concurrent no treatment
Method : other
Year : 1975
GLP : no data
Test substance :

Attached document : Rat 14-Day Inhalation

In a 14-day inhalation study, no systemic toxicity was observed in rats treated with up to 18 mg/L. Rats were exposed to an atmosphere of 0, 2, 6 or 18 mg micronized TBBPA/L air (0, 2000, 6000, or 18,000 mg/m3) for 4 h daily, 5 days/week for 2 weeks. Mortality, body weight gain, food

consumption, hematological, biochemical or urinary parameters were not affected by treatment. No gross or microscopic lesions were detected in any dose level. (Goldenthal et al. 1975; WHO 1995)

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
12.08.2005 (70) (14)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Chromosomal aberration test
System of testing : human peripheral lymphocytes
Test concentration : see attached document
Cycotoxic concentr. : see attached document
Metabolic activation : with and without
Result : negative
Method : EPA OPPTS 870.5375
Year : 2001
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : Chromosome Aberration Test

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and OECD guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel.

TBBPA was tested in the in vitro mammalian chromosome aberration test using human peripheral lymphocytes (HPBL) in both the absence and presence of an Arochlor-induced S9 activation system. Dose levels in the definitive assay in absence of exogenous metabolic activation (4 hr treatment, 20 hr harvest) were 6.25, 25, 100 ug/ml, and for a 20 hr treatment, 20 hr harvest were 6.25, 25, 75 ug/ml. In the presence of metabolic activation (4 hr treatment, 20 hr harvest), test article concentrations were 3.125, 12.5, 50 ug/ml.

The test article was soluble in treatment medium at all concentrations tested. Toxicity (mitotic inhibition) was appr. 54 and 59% at the highest dose level evaluated for chromosome aberrations, 100 ug/ml and 75 ug/ml in the non-activated 4 hr and 20 hr exposure groups, respectively. Toxicity (mitotic inhibition) was 58% at the highest dose level evaluated for chromosome aberrations, 50 ug/ml, in the S9 activated study.

No statistically significant increases in structural and numerical chromosome aberrations were observed in the non-activated or the S9 activated 4 hr exposure groups relative to the solvent control group, regardless of dose level ($p>0.05$, Fisher's exact test). In the absence of a positive response in the non-activated 4 hr exposure group, the non-activated 20 hr continuous exposure group was evaluated for structural and numerical chromosome aberrations. No statistically significant increases in structural and numerical chromosome aberrations were observed in the non-activated 20 hr continuous exposure group relative to the solvent control group, regardless of dose level ($p>0.05$, Fisher's exact test). The positive controls performed as expected.

TBBPA was negative for the induction of structural and numerical chromosome aberrations in the in vitro chromosome aberration test using human peripheral lymphocytes.

Reliability : (1) valid without restriction

Flag : Risk Assessment, Critical study for SIDS endpoint
11.08.2005 (71)

Type : Ames test
System of testing : see attached document
Test concentration :
Cycotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method :
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Attached document : TBBPA has been tested in multiple Ames assays. All results were negative for mutagenicity. See WHO 1995 for details.

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
11.08.2005 (14)

Type : other
System of testing : Sp5 and SPD8 cell lines
Test concentration : see attached document
Cycotoxic concentr. : see attached document
Metabolic activation :
Result : negative
Method : other
Year : 1999
GLP : no
Test substance : other TS

Attached document : The Sp5 and SPD8 cell lines were developed by the paper's authors. The clones used in this study exhibit spontaneous partial duplication of the hprt gene, resulting in a non-functional hgprt protein. These mutants revert spontaneously to a functional hprt gene phenotype by recombination with a frequency of 1 x 105 reversions/cell generation. This reversion frequency is said to increase by exposure to chemical or physical agents. Treatment with the test substance was for 24 hr.

In the SPD8 cells, TBBPA concentrations of 0, 5, 10, 20, 30, and 40 ug/ml resulted in a reversion frequency of 1.0, 1.1, 1.4, 1.3, 1.3, and 1.0, respectively. Cytoxicity was not observed at the doses tested. In the Sp5 cells, TBBPA concentrations of 0, 10, 20, 40, 70 ug/ml resulted in a reversion frequency of 1.0, 0.8, 0.8, 1.0 and 0.7, respectively. Cytotoxicity was observed at 70 ug/ml. None of these reversion frequencies were statistically different from the control (Student's t test, $p<0.05$). Thus, TBBPA had no effect in either the SPD8 or Sp5 recombination assay

Reliability : (4) not assignable
04.04.2005 (72)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type	:	other
Species	:	
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Frequency of treatm.	:	
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	
No. of generation studies	:	
Doses	:	
Control group	:	
Attached document	:	Several developmental toxicity studies on TBBPA (Section 5.8.2) are available, one of which was recently completed under current guidelines and Good Laboratory Practices using the TBBPA in commercial production and use at a top dose of 1,000 mg/kg/d. All studies are negative for developmental toxicity. Several repeated dose studies (Section 5.4), in more than one mammalian species, are also available and none show evidence of an effect on the reproductive tract. According to the SIDS Manual, when teratology and 90 day studies show no effects on the reproductive system then the requirement for the reproductive endpoint are met. In addition, a rat two-generation reproduction study (Section 5.8.3) found a no effect level (NOEL) of 1000 mg/kg/d for reproductive performance and pup toxicity. Thus, the weight of the evidence indicates TBBPA does not affect fertility or reproduction
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

12.08.2005 (66) (73) (74)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	day 0-19 of gestation
Frequency of treatm.	:	once daily
Duration of test	:	throughout gestation
Doses	:	100, 300, 1,000 mg/kg body wt
Control group	:	yes, concurrent vehicle
NOAEL maternal tox.	:	= 1000 mg/kg bw
NOAEL teratogen.	:	= 1000 mg/kg bw
Result	:	not a developmental toxicant; not maternally or fetally toxic
Method	:	EPA OPPTS 870.3700
Year	:	2001
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : Rat Prenatal Developmental

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS and OECD guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel (BFRIP)

The objective of this study was to provide information concerning the effects of oral treatment of the pregnant rat with TBBPA on the developing organism. This included death, structural abnormalities or altered growth, and assessment of maternal effects. This study consisted of 3 treatment groups and 1 vehicle (corn oil) control group (25 mated female rats/group). Female CD® rats [Crl: CD® (SD) IGS BR] were mated in-house and received TBBPA at dose levels of 0, 100, 300 and 1000 mg/kg/d at a constant volume of 5ml/kg. The control animals received the vehicle at the same volume and dosing regimen as the treated groups. The test article was administered orally by gavage as a single daily dose. Dosing initiated on Day 0 of gestation and continued through to include Day 19 of gestation. The day on which evidence of mating was observed was considered Day 0 of gestation. Observations of the dams included clinical signs, gestational body weights, and food consumption. Females were euthanized on Day 20 of gestation and given a postmortem macroscopic examination. Gross lesions were saved in 10% neutral buffered formalin for possible future examination. Gravid uterine weights and liver weights were recorded. Litters were delivered by cesarean section. The total number of corpora lutea, uterine implantations, early and late resorption, viable and nonviable fetuses, and the sex and individual weights of fetuses were recorded. Al fetuses were given a gross external examination for malformations and variations. Approximately one-half of the fetuses in each litter were fixed in Bouin's solution, and the remaining fetuses were skinned and preserved in alcohol. Bouin's-fixed fetuses from the control and all treated groups were examined for visceral abnormalities (freehand razor blade sectioning procedure), and the remaining fetuses from all groups were stained with Alizarin Red S and Alcian Blue and evaluated for skeletal/cartilaginous malformations and ossification variations. The maternal Day 20 gestation examinations and cesarean sections and subsequent fetal evaluations were performed blind to treatment.

Pretest analyses confirmed that the suspensions as prepared were homogeneous and stable for a t least 14 days when stored refrigerated. Periodic analysis of the dosing suspensions showed levels ranged from 88 - 113% of nominal and confirmed that animals were receiving the appropriated dose levels.

No test article-related mortality occurred. The death of 1 animal in the 300 mg/kg/day group on Gestation Day 5 was due to an intubation injury. All other animals survived to scheduled euthanasia.

Salivation was seen among the TBPPA-treated animals, occurring most frequently at the 300 an 1000 mg/kg/day dose levels. Because of its sporadic occurrence, this was not considered to represent a direct effect of TBBPA, but more likely was in response to the taste of the residual amounts of the test article on the dosing catheter. No other effects of treatment were seen on clinical examination. No effect of treatment was evident from gestational parameters (body weight, body weight gain, or food consumption), uterine implantation data, liver weights, or necropsy findings. No effect of treatment was evident on fetal body weights, fetal sex distribution, or on fetal external, visceral or skeletal examinations. The NOAEL in this oral developmental toxicity study in rats with TBBPA for maternal and developmental toxicity was 1000 mg/kg/d, the highest dose

level tested.

Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment, Critical study for SIDS endpoint

10.08.2005 (74)

Species	:	rat
Sex	:	female
Strain	:	other: Charles River CD
Route of admin.	:	gavage
Exposure period	:	day 6-15 of gestation
Frequency of treatm.	:	once daily
Duration of test	:	as under exposure period
Doses	:	30, 100, 300, 1,000, 3,000, or 10,000 mg/kg body weight
Control group	:	yes, concurrent vehicle
NOAEL maternal tox.	:	= 3000 mg/kg bw
NOAEL teratogen.	:	= 3000 mg/kg bw
Result	:	NOEL=3000 mg/kg bw
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : Rat Prenatal Developmental

TBBPA was administered by gavage at dose levels of 0, 30, 100, 300, 1,000, 3,000, or 10,000 mg/kg body weight on gestation days 6-15 to pregnant rats. No signs of toxicity were observed in rats receiving doses of 3,000 mg/kg or less. No differences in the mean numbers of viable or nonviable fetuses, resorption, implantations, or corpora lutea were detected between treated and control rats.

Reliability	:	(2) valid with restrictions
Flag	:	Risk Assessment, Critical study for SIDS endpoint

11.08.2005 (75) (14)

Species	:	rat
Sex	:	female
Strain	:	Wistar
Route of admin.	:	oral unspecified
Exposure period	:	0-19 of gestation
Frequency of treatm.	:	once daily
Duration of test	:	as above
Doses	:	280, 830, 2500 mg/kg bw
Control group	:	yes
NOAEL maternal tox.	:	= 2500 mg/kg bw
NOAEL teratogen.	:	= 2500 - mg/kg bw
Result	:	Not a developmental toxicant
Method	:	other
Year	:	1985
GLP	:	no data
Test substance	:	

Attached document : Rat Developmental

Female rat were treated with TBBPA at doses of 0, 280, 830, or 2,500 mg/kg body weight from day 0-19 of gestation for fetal examination or to parturition for postnatal examination (21 days post-birth). Cesarian sections wree performed on day 20 of gestation.

In dams, TBBPA didnot affect the rate of prgancy or parturition. In fetuses, TBBPA did not induce embryo/fetal toxicity, and no external, skeletal or visceral anomalies ewre deteced. No adverse change was observed in the postnatl development (21 days post birth) of the offspring of any group.

The maternal, fetal and neonatal NOAEL was 2,500 mg TBBPA/kg/d, the highest dose tested.

The reference is written in Japanese with only the data tables and abstract available in English. The lack of toxicity in this study at 2,500 mg/kg bw is consistent with the 2001 BFRIP study.

Reliability : (2) valid with restrictions
Flag : Risk Assessment, Critical study for SIDS endpoint
10.08.2005 (76)

Species : mouse
Sex : male
Strain : NMRI
Route of admin. : gavage
Exposure period : single dose PND 10
Frequency of treatm. : once
Duration of test : single dose PND 10
Doses : 0.75, 11.5 mg
Control group : yes
Result : No effect on spontaneous behavior or swim maze performance
Method : other
Year : 1998
GLP : no
Test substance : other TS: purchased from Aldrich and recrystallized from chloroform

Attached document : Mouse Developmental Neurotoxicity

Methodology developed by the paper's authors. TBBPA (0.75 or 11.5 mg) was administered as a single oral dose to neonatal mice (n=8) on postanal day 10. The vehicle was a 20% fat emulsion.

At 2 and 4 months of age, the mice were evaluated for spontaneous behavior: locomotion (horizontal movement), rearing (vertical movement) and total activity (all types of vibration within the test cage, e.g. those caused by mouse movements and groming).

At 5 months of age, the mice were evaluated in a swim maze (Morris water maze type). The mice's ability to find a submerged platform was studied for 5 days.

No clinical signs of toxicity were observed. No effect on weight gain.

No effects on spontaneous behavior or swim maze performance in mice tested at 2, 4, or 5 months of age.

This is a nonstandard test. The reliability and reproducability of the results are unknown.

Sponsor: grants from the Swedish Environmental Protection Board and the Foundation for Strategic Environmental Research.

Reliability : (4) not assignable
10.08.2005 (77)

04.04.2005

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

Type : other

In vitro/in vivo	:	In vivo
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	see attached document
Frequency of treatm.	:	Once daily, 7 d/wk
Duration of test	:	two generations
Doses	:	10, 100 and 1,000 mg/kg body wt
Control group	:	yes, concurrent vehicle
Result	:	did not affect reproduction at 1,000 mg/kg; see attached document
Method	:	other: EPA OPPTS Method 870.3800
Year	:	2002
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Attached document : Rat 2-Generation Reproduction Study (BFRIP)

This study was conducted using a composite of the commercial products produced by Albemarle Corporation, Dead Sea Bromine Group, and Great Lakes Chemical Corporation. It was performed according to Good Laboratory Practices and according to US EPA OPPTS guidelines. Sponsor: ACC Brominated Flame Retardant Industry Panel (BFRIP)

The objective of this reproduction study was to provide information concerning the effects of TBBPA over the course of two generations (P and F1) and the growth and development of the offspring (F1 and F2. A developmental neurotoxicity/neuropathology assessment was also conducted on the F2 offspring. The study consisted of three treatment groups (10, l00 and 1000 mg/kg/day) and a vehicle (corn oil)-treated control group (30 CD® [Crl: CD® (SD) IGS BR] Sprague-Dawley rats/sex/group/generation). TBBPA was administered orally via gastric intubation. Animals were treated seven days a week throughout the study. Dosing suspensions were prepared fresh weekly. Parental animals were treated for at least 10 weeks prior to mating (premating treatment period) to produce the F1 and F2 litters. In the developmental neurotoxicity/neuropathology (DNT/NP) component, F2 pups were randomly selected to continue on study for the following evaluations (unique sets of animals [10 pups/sex/group] were randomly selected for each assessment): PND 60 brain weights, PND 60 perfusion and neuropathology, special detailed clinical examinations (PND 4, 11, 21, 35, 45, and 60), motor activity [MA] (PND 13, 17, 21, and 60), auditory startle habituation [ASH] (PND 22 and 60), and learning and memory [L&M] (PND 22, 60 and 110). Additionally, 10 F2 pups/sex/group were selected randomly on PND 11 for collecting, weighing, and preserving of the brains.

For breeding of the P and F1 generations, one male was paired with one female from the same treatment group continuously until mating occurred or for 14 consecutive days. The day of mating evidence was considered Day 0 of gestation. During mating of the F1 generation, cohabitation of littermates was avoided. Females delivered and nursed litters over a 21-day lactation period. On Day 4 of lactation all litters were culled if necessary to 8 pups (F1) or 10 pups (F2) with sex distribution equalized, when possible. Litters with fewer pups than required at culling were not adjusted.

At weaning of each F1 litter, at least one pup/sex/litter was selected to continue on study as the F1 parental generation (30 pups/sex/group). These pups started treatment on PND 22. The premating period formally initiated after the last litter weaned. Thus, there was a maximum of two weeks difference in age for the F1 animals within each treatment group at initiation of the premating growth period.

Detailed clinical examinations, body weights, and food consumption were recorded periodically throughout the study for the P and F1 parental animals. Estrous cyclicity was
evaluated in the P and F1 females the last three weeks of the premating period, and these evaluations continued until the female was confirmed mated or to the end of the mating period. Females were allowed to deliver and nurse the litter to weaning. Litters were evaluated at birth and throughout the lactation period. Each pup was individually identified at birth (paw tattoo), sexed, examined externally for defects, and weighed. All pups were monitored for appearance, growth, and survival throughout the lactation period. Clinical examinations, body weights, food consumption, and occurrence of maturation landmarks (vaginal opening [VO] and preputial separation [PS]) were recorded for F) parental animals.

Several days before terminal euthanasia of the P and F1 animals, blood was collected from 10 randomly selected animals/sex/group and analyzed for thyroid hormone levels (TSH, T 3 and T 4). At necropsy, P and F1 animals received a macroscopic examination and reproductive tissues and other designated tissues were taken, weighed, and preserved. Reproductive tissues were evaluated microscopically for all P and F1 animals in the control and 1000 mg/kg/day groups. Microscopic examinations were also performed for reproductive tissues of the few low- and mid-dose P and F1 animals that failed to mate, conceive or sire. Gross lesions were also examined microscopically for all parental animals. Sperm evaluations (motility, caudal epididymal sperm counts, homogenization-resistant testicular sperm head counts, and morphology) for P and F, males and a count of primordial follicles were conducted for P and F1 females. The latter evaluations were conducted only in the control and 1000 mg/kg/day groups. At weaning, the unselected F1 pups and one F2 pup/sex/litter were euthanized, necropsied, specific organs weighed (brain, spleen, and thymus), and gross lesions preserved.

In the DNT/NP component, brains from F2 pups euthanized on PND 11 (l0/sex/group) were weighed, and preserved in fixative for neuropathological evaluation and morphometric measurements. These examinations were initially conducted in the control and high-dose animals and were expanded to include the lower dose groups. F 2 pups retained post-weaning were observed twice daily cage side for mortality and were weighed and given detailed clinical examinations periodically during the study. Sexual maturation (VO and PS) was evaluated for the 40 animals/sex/group retained for the neurobehavioral assessments (i.e., special clinical examinations, MA, L&M, and ASH). These animals were euthanized after all the behavioral tests had been completed. At termination, all F2 animals were weighed, given a detailed clinical examination and necropsied. The F2 animals euthanized on PND 60 for neuropathological evaluation were anesthetized with sodium pentobarbital and perfused with 3% paraformaldehyde and 3% glutaraldehyde. The whole brain, sections of the spinal cord, and selected peripheral nerves were collected and processed for neuropathological examination in the control and 1000 mg/kg/day groups.

Dosing formulations were homogeneous at the batch size prepared and stable when refrigerated to 14 days. Mean recoveries from the periodic analyses of dosing suspensions used on study were 101 %, 99%, and 105% of nominal for the 10, l00, and 1000 mg/kg/day groups, respectively.

No effect of treatment was seen for mortality in the P and F1 generations. The low incidence of mortality seen in these animals was considered incidental and unrelated to treatment with TBBPA.

In the parental generations, the only effect of treatment with TBBPA was

seen in the F1 males at 1000 mg/kg/day and involved lower body weights for several weekly intervals during the study and lower weight gain over the entire Week 1-11 premating period. No effect of treatment in either generation was evident from the clinical examinations, estrous cyclicity, reproductive performance, gestation/lactation body weights or food consumption, gestation length, litter data, or from the macroscopic and microscopic evaluations, organ weights, sperm evaluations, and primordial follicle counts. No effect on body weights or body weight gain was seen in the P animals or F1 parental females. Likewise, no adverse effect on food consumption was seen in the treated groups for either generation.

No effect of treatment with TBBPA was evident in the F, and F2 pups in regard to body weights, clinical findings, sex ratios, survival to weaning, macroscopic findings, or organ
weight data (Day 21).

No effects on thyroid hormone levels (TSH, T3 and T4) were observed at the 10 mg/kg/day dose level in either generation. At 100 and 1000 mg/kg/day, some treatment-related effects on some thyroid hormone parameters (T3 and T4) were seen. TSH levels were unaffected, however, in either generation. Treatment with TBBPA demonstrated an increased incidence and magnitude of lower T4 values in the l00 and 1000 mg/kg/day groups. P males given 1000 mg/kg/day, and F, males given 100 or 1000 mg/kg/day also had mild reductions in T3 values. In the absence of increases in TSH hormone levels, moderate reductions in circulating serum T4 levels, with only mild decreases in T3 for a few 1000 mg/kg/day P males, and l00 and 1000 mg/kg/day F, males, are suggestive of induction of hepatic T4-uridine diphosphate glucuronyl transferase (UDP-GT) enzymes that increase the removal of thyroxine. TBBPA has been shown in vitro to competatively displace T4 from human transthyretin, a serum carrier protein. The decreases in T4 and T3 observed in this study did not exceed the threshold for stimulation of TSH production. Thus, repeat daily dosing with TBBP A at doses of l00 or 1000 mg/kg/day to P and F1 generation rats resulted in effects on thyroid function, probably secondary to enzyme induction, without alteration in TSH activity. The 10 mg/kg/day dose was determined to be a no observed effect level (NOEL) for TBBPA and its response on thyroid function.

In the DNT/NP component, no effects of treatment were seen in F2 pups with respect to: PND 60 brain weights, PND 60 perfusion and neuropathology, special detailed clinical examinations (PND 4, 11, 21, 35, 45, and 60), motor activity (PND 13, 17, 21, and 60), auditory startle habituation (PND 22 and 60), and learning and memory (PND 22, 60 and 110). The only suggestion of a treatment-related effect was a reduction in the thickness of the parietal cortex of Day 11 pups at the 1000 mg/kg/day dose level, but not in pups at this dose level on Day 60. This change on Day 11 was not accompanied by any histologic changes in the parietal cortex, such as degeneration, necrosis, cell loss, demyelination, proliferative changes, or changes in neuronal cell density. A likely explanation for the decreased thickness of parietal cortex would be a decreased number of cells without changes in cell density. The brain weights of the 11-day-old rats were virtually equal across groups. However, it is possible that other regions of the brain were enlarged and compensated for the decrease in the thickness of parietal cortex in the affected groups. The thickness of the parietal cortex for the animals at the 10 and l00 mg/kg/day dose levels was comparable to the control. No microscopic alterations were observed in brain, spinal cord, nerves, and ganglia in the 60-day-old rats. Therefore, this apparent test-article related effect in the Day 11 F2 pup brains must be interpreted with caution, given the limitations of morphometric analysis. No effect of treatment was evident from the other parameters evaluated in the DNT/NP component. This would include the special detailed clinical observations, developmental

maturation landmarks (vaginal opening and preputial separation), neurobehavioral evaluations (motor activity, learning and memory, auditory startle habituation), or Day 60 brain weights or parietal cortex thickness.

Thus, in this 2-generation reproduction study with TBBPA the No Observed Effect Level (NOEL) for parental toxicity was 100 mg/kg/day based on lower body weights and body weight gain in males at the 1000 mg/kg/day dose level. The NOEL for effects of TBBPA on thyroid hormone levels was 10 mg/kg/day based on lower T3 and T4 levels at the l00 and mg/kg/day dose levels. TSH levels, however, were not affected at any of the dose levels in either generation. The NOEL for reproductive performance and pup toxicity was 1000 mg/kg/day, the highest dose level evaluated. In the DNT/NP component, the NOEL was l00 mg/kg/day based on subtle morphometric changes in the parietal cortex in the brains of the Day 11 F2 pups, but not Day 60 F2 pups, in the 1000 mg/kg/day group. In this component no changes at any dose level were seen in the pups at any time point from clinical findings, sexual maturation landmarks, growth, or from the various behavioral assessments. (Schroeder R. 2002. An oral two generation reproductive, fertility, and developmental neurobehavioral study of tetrabromobisphenol A in rats. Study ID Number: 474-004. MPI Research, Inc. Mattawan, MI.)

Reliability : (1) valid without restriction
Flag : Risk Assessment, Critical study for SIDS endpoint
11.08.2005 (73)

5.9 SPECIFIC INVESTIGATIONS

Endpoint : other: in vitro estrogenic properties in human breast cancer cell line
Study descr. in chapter :
Reference : Samuelsen et al. 2001. Cell Biology and Toxicology 37:139-151.
Type : other:competition with estradiol for binding to estrogen receptor
Species : human
Sex :
Strain :
Route of admin. : in vitro cell culture
No. of animals :
Method : other
Year : 2001
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Attached document : In Vitro Binding to Estrogen Receptor in Human Breast Cancer Cell Line

The estrogenic potency of TBBPA in the estrogen-depended human breast cancer cell line MCF-7 was investigated. The relative binding affinity of TBBPA compared to 17B-estradiol (RBA=100) was 0.004. The relative proliferative potency of TBBPA compared to 17B-estradiol (RPP=100) was >0.000003. Strong binding to serum proteins during incubation was found to reduce TBBPA's access to the estrogen receptors.

Thus, TBBPA had essentially no estrogenic activity compared to 17B-estradiol in this system (Samuelsen et al 2001).

11.08.2005 (78)

5.10 EXPOSURE EXPERIENCE

Type of experience : other: Detection in Humans

Attached document : A few studies have reported analyzing human tissue samples for TBBPA content (Hagmar et al. 2000; Jakobsson et al. 2002; Klassen Wheler et al. 1997; Thomsen et al. 2002; Hayama et al. 2004). Without exception, where detected, the levels reported were extremely small. For example, Hagmar et al. reported TBBPA sera concentations in four workers in a Swedish electronics dismantling plant of 2-7 pmol/g lipid, and estimated TBBPA's half-life to be 2.2 days. Jakobsson et al. reported detecting TBBPA in sera of 8 out of 10 computer technicians in Sweden (median < 1 pmol/g lipid; range <1-3.4 pmol/g lipid), but also stated that data was available from only half of the samples analyzed "since the interfernce level was higher in some of the blank samples analyzed giving a higher LOQ for these samples". In archived serum samples from Norway, all concentrations were below the limit of quantitation and < 1 pmol/g lipid or < 0.006 ng/ml serum (Thomsen et al).

TBBPA and other bromianted flame retardants in laboratory air (Thomsen et al. 2001). In order to avoid contamination, attention must be paid to the principals of trace analyis. In particular, all glassware must be properly cleaned and direct exposure to laboratory air minimized (Thomsen et al. 2001).

Given TBBPA's rapid metabolism and excretion and the failure to detect TBBPA in blood plasma after intentional oral exposure to human volunteers (Section 5.0), these reports of detection of trace amounts of TBBPA in humans are questionable. Further, the amounts reported are below any concern especially when TBBPA's general lack of mammalian toxicity is considered.

12.08.2005 (79) (80) (81) (82) (21) (83)

5.11 ADDITIONAL REMARKS

Type : other: Summary Mammalian Toxicology

Attached document : TBBPA is not acutely toxic or irritating to the skin and eye. It does not illicit delayed skin hypersensitivity. It is not a developmental toxicant and does not affect reproduction at doses up to 1000 mg/kg bw. It produces essentially no adverse effects when administered repeatedly at doses up to 1000 mg/kg/d. It is rapidly metabolized and eliminated as glucuronide and sulfate conjugates, and is not expected to bioaccumulate.

12.08.2005

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT